

GenCore version 5.1.6
Copyright (c) 1993 - 2005 CompuGen Ltd.

OM protein - protein search, using sw model

Run on: April 12, 2005, 14:21:26 ; Search time 181 Seconds
(without alignments)
1378.235 Million cell updates/sec

Title: US-10-082-747A-93

Perfect score: 3347

Sequence: 1 MSERKEGRGKGKKKRGSS.....QBEIQALSSVIANODPIAV 645

Scoring table: BLOSUM62

Gapop 10.0 , Gapext 0.5

Searched: 2105692 seqs, 386760381 residues

Total number of hits satisfying chosen parameters: 2105692

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : A_Geneseq_16Dec04:*

1: Geneseqp1980s:*

2: Geneseqp1990s:*

3: Geneseqp2000s:*

4: Geneseqp2001s:*

5: Geneseqp2002s:*

6: Geneseqp2003as:*

7: Geneseqp2003bs:*

8: Geneseqp2004s:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	DB ID	Description
1	3347	100.0	645	2	Aay06635 Herugelin
2	3347	100.0	645	3	Aab36793 Human her
3	3347	100.0	645	7	Adb67619 Human her
4	3347	100.0	645	8	Adn48871 Human her
5	3347	100.0	675	2	Aar29571 Human her
6	3347	100.0	675	3	Aay71172 Human her
7	3347	100.0	675	4	Aau09887 Human her
8	3344	99.9	675	3	Aay71198 Human her
9	3344	99.9	675	3	Aay71188 Human her
10	3344	99.9	675	3	Aay71189 Human her
11	3344	99.9	675	3	Aay71191 Human her
12	3343	99.9	675	3	Aay71182 Human her
13	3343	99.9	675	3	Aay71203 Human her
14	3343	99.9	675	3	Aay71194 Human her
15	3342	99.9	675	3	Aay71180 Human her
16	3342	99.9	675	3	Aay71185 Human her
17	3342	99.9	675	3	Aay71197 Human her
18	3341	99.8	675	3	Aay71186 Human her
19	3341	99.8	675	3	Aay71183 Human her
20	3341	99.8	675	3	Aay71190 Human her
21	3341	99.8	675	3	Aay71181 Human her
22	3341	99.8	675	3	Aay71187 Human her
23	3341	99.8	675	3	Aay71201 Human her
24	3341	99.8	675	3	Aay71184 Human her
25	3340	99.8	675	3	Aay71192 Human her

26	3340	99.8	675	3	AAy71202	Human Her
27	3340	99.8	675	3	AAy71200	Human Her
28	3340	99.8	675	3	AAy71195	Human Her
29	3340	99.8	675	3	AAy71178	Human Her
30	3339	99.8	675	3	AAy71196	Human Her
31	3338	99.7	675	2	AAW74494	Amino aci
32	3338	99.7	675	3	AAy71193	Human Her
33	3338	99.7	675	3	AAy71179	Human Her
34	3338	99.7	675	3	AAy71199	Human Her
35	3337	99.7	645	4	AAg67911	Human NRG
36	3337	99.7	645	4	AAg67949	Human NRG
37	3335	99.6	675	2	AAW74493	Amino aci
38	3332	99.6	675	2	AAW74509	Amino aci
39	3327	99.4	675	2	AAW74503	Amino aci
40	3322	99.3	675	2	AAW74488	Amino aci
41	3319	99.2	675	2	AAW74500	Amino aci
42	3316	99.1	675	2	AAW74489	Amino aci
43	3316	99.1	675	2	AAW74491	Amino aci
44	3312	99.0	675	2	AAW74487	Amino aci
45	3312	99.0	675	2	AAW74496	Amino aci

ALIGNMENTS

RESULT 1
AAY06635
ID AAY06635 standard; protein; 645 AA.
XX AC AAY06635;
XX DT 26-OCT-1999 (first entry)
XX DE Herugelin-beta-1.
XX KW Hergulin-beta-1; HRG-alpha; human; ligand; HER2; HER3; HER4; receptor;
XX KW lung surfactant; respiratory distress syndrome; emphysema;
XX KW epithelial growth factor; therapy.
XX OS Homo sapiens.
XX PN WO9939729-A2.
XX PD 12-AUG-1999.
XX PF 03-FEB-1999; 99WO-US002390.
XX PR 04-FEB-1998; 98US-00020598.
XX (GETH) GENENTECH INC.
XX (IOWA) UNIV IOWA RES FOUND.
XX PI Sliwkowski M, Kern JA;
XX DR WPI; 1999-494213/41.
XX DR N-PSDB; AAX87701.
XX PT Herugelin ligands can be used to induce epithelial cell growth, and to
XX PT promote repair and healing of tissue damage or injury.
XX PS Disclosure; Page 87-90; 120pp; English.
XX CC This sequence represents heregulin-beta-1 (HRG-beta-1) deduced from HRG-
XX CC beta-1 cDNA (see AAX87701). The invention provides HRG ligands, including
XX CC HRG-beta-1, that have affinity for and stimulate HER2, HER3 and/or HER4
XX CC receptors in autophosphorylation. A new method of treating respiratory
XX CC distress syndrome in humans uses HER2, HER3 and/or HER4 receptor ligands
XX CC as epithelial growth factors. A novel method of inducing epithelial cell
XX CC growth and/or proliferation comprises contacting a normal epithelial cell
XX CC which expresses HER2, HER3 and/or HER4 receptors with an isolated ligand
XX CC which activates HER2, HER3, HER4 receptors or their combination. Also
XX CC claimed are methods of increasing lung surfactant protein A, or of
XX CC treating chronic obstructive pulmonary disease, respiratory distress or

CC emphysema, by administering an effective amount of an isolated HER ligand
 CC to a patient
 XX
 SQ Sequence 645 AA;

Query Match 100.0%; Score 3347; DB 2; Length 645;
 Best Local Similarity 100.0%; Pred. No. 2.2e-204;
 Matches 645; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MSERKEGRGKGKKGKVERSGKPKESAGSQSPALPOLKEMKQSAAGSKLVLRCTS 60
 DB 1 MSERKEGRGKGKKGKVERSGKPKESAGSQSPALPOLKEMKQSAAGSKLVLRCTS 60
 QY 61 SEYSSLRFRKFKNGELNRKNKPNQIKIQQKPKSELINKASLADSGEYMKVSKLGN 120
 DB 61 SEYSSLRFRKFKNGELNRKNKPNQIKIQQKPKSELINKASLADSGEYMKVSKLGN 120
 QY 121 DSANANITIVESNEIITGMPASTEGAYVSESPRISVSTEGANTSSSTSTSTGTGSHLV 180
 DB 121 DSANANITIVESNEIITGMPASTEGAYVSESPRISVSTEGANTSSSTSTSTGTGSHLV 180
 QY 181 KCAEKEKTCVNGGECFVMDLSNPSRYLCKPNEFTGDRCONYVNASFYKHLGIEFMEA 240
 DB 181 KCAEKEKTCVNGGECFVMDLSNPSRYLCKPNEFTGDRCONYVNASFYKHLGIEFMEA 240
 QY 241 EELYQKRVLTITGICALLVVGIMCVVAYCKTKQKPKSELINKASLADSGEYMKVSKLGN 300
 DB 241 EELYQKRVLTITGICALLVVGIMCVVAYCKTKQKPKSELINKASLADSGEYMKVSKLGN 300
 QY 301 PHPNPPPPENVQVNVQVSKNVISSHEIIVERAEATSFSTSHYTSTAHHSTTTVTPSHSW 360
 DB 301 PHPNPPPPENVQVNVQVSKNVISSHEIIVERAEATSFSTSHYTSTAHHSTTTVTPSHSW 360
 QY 361 SNGHTESILSESHSVIWMSSVENSRHSPTGPGRLNGTGGPRECNPSLRHARETPOSY 420
 DB 361 SNGHTESILSESHSVIWMSSVENSRHSPTGPGRLNGTGGPRECNPSLRHARETPOSY 420
 QY 421 RDSPHSERVVSAMTTPARMSVDPDFTHTSPSPKSPPEMSPPVSSMTVSPMSMAVSPFMBEE 480
 DB 421 RDSPHSERVVSAMTTPARMSVDPDFTHTSPSPKSPPEMSPPVSSMTVSPMSMAVSPFMBEE 480
 QY 481 RPLLLVTPPRLREKKFDHHPQOFSSFHNNPAHDSNSLPASPLRIVEDEEYETTQYEPQAQ 540
 DB 481 RPLLLVTPPRLREKKFDHHPQOFSSFHNNPAHDSNSLPASPLRIVEDEEYETTQYEPQAQ 540
 QY 541 EPVKKLANSRRAKRTKPNGHIANRLEVDNSTSSQSNSESETEDEDERVGEDTFFLGIQNPL 600
 DB 541 EPVKKLANSRRAKRTKPNGHIANRLEVDNSTSSQSNSESETEDEDERVGEDTFFLGIQNPL 600
 QY 601 AASLEATPAFLADSRTPNAGRFSTQBEIQARLSSVIANQDPIAV 645
 DB 601 AASLEATPAFLADSRTPNAGRFSTQBEIQARLSSVIANQDPIAV 645

RESULT 2

AAB36793

ID AAB36793 standard; protein; 645 AA.

XX

AC AAB36793;

XX

DT 16-FEB-2001 (first entry)

DE

XX Human heregulin-beta1 residues 175-230.

DE

XX Heregulin; ErbB receptor; transplantation; cancer;

KW nervous system disease; musculature; epithelium.

XX

OS Homo sapiens.

XX

PN US6136558-A.

XX

PD 24-OCT-2000.

XX

PP 09-FEB-1998; 98US-00020880.
 XX
 PR 10-FEB-1997; 97US-0037581P.
 XX
 PA (GETH) GENENTECH INC.
 XX Jones JT, Fairbrother WJ, Ballinger MD, Wells JA, Sliwkowski MX;
 PI
 XX WPI; 2000-678767/66.
 DR
 XX New variants of heregulin, useful e.g. for treating cancer, comprises
 PT specific amino acid alterations that increase affinity for ErbB
 PT receptors.
 XX
 XX Claim 9; Col 81-86; 58pp; English.
 XX
 CC The present invention relates to variants of heregulin that can bind to
 CC an ErbB receptor and include a portion of the 175-230 region of native
 CC human heregulin-beta1. The variants may be used to promote ex vivo
 CC survival, proliferation and differentiation of cells, particularly when
 CC intended for transplantation. They may also be used to treat a wide range
 CC of cancers and diseases of the nervous system, musculature and epithelium
 XX
 SQ Sequence 645 AA;
 Query Match 100.0%; Score 3347; DB 3; Length 645;
 Best Local Similarity 100.0%; Pred. No. 2.2e-204;
 Matches 645; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
 QY 1 MSERKEGRGKGKKGKVERSGKPKESAGSQSPALPOLKEMKQSAAGSKLVLRCTS 60
 DB 1 MSERKEGRGKGKKGKVERSGKPKESAGSQSPALPOLKEMKQSAAGSKLVLRCTS 60
 QY 61 SEYSSLRFRKFKNGELNRKNKPNQIKIQQKPKSELINKASLADSGEYMKVSKLGN 120
 DB 61 SEYSSLRFRKFKNGELNRKNKPNQIKIQQKPKSELINKASLADSGEYMKVSKLGN 120
 QY 121 DSANANITIVESNEIITGMPASTEGAYVSESPRISVSTEGANTSSSTSTSTGTGSHLV 180
 DB 121 DSANANITIVESNEIITGMPASTEGAYVSESPRISVSTEGANTSSSTSTSTGTGSHLV 180
 QY 181 KCAEKEKTCVNGGECFVMDLSNPSRYLCKPNEFTGDRCONYVNASFYKHLGIEFMEA 240
 DB 181 KCAEKEKTCVNGGECFVMDLSNPSRYLCKPNEFTGDRCONYVNASFYKHLGIEFMEA 240
 QY 181 KCAEKEKTCVNGGECFVMDLSNPSRYLCKPNEFTGDRCONYVNASFYKHLGIEFMEA 240
 DB 181 KCAEKEKTCVNGGECFVMDLSNPSRYLCKPNEFTGDRCONYVNASFYKHLGIEFMEA 240
 QY 241 EELYQKRVLTITGICALLVVGIMCVVAYCKTKQKPKSELINKASLADSGEYMKVSKLGN 300
 DB 241 EELYQKRVLTITGICALLVVGIMCVVAYCKTKQKPKSELINKASLADSGEYMKVSKLGN 300
 QY 301 PHPNPPPPENVQVNVQVSKNVISSHEIIVERAEATSFSTSHYTSTAHHSTTTVTPSHSW 360
 DB 301 PHPNPPPPENVQVNVQVSKNVISSHEIIVERAEATSFSTSHYTSTAHHSTTTVTPSHSW 360
 QY 361 SNGHTESILSESHSVIWMSSVENSRHSPTGPGRLNGTGGPRECNPSLRHARETPOSY 420
 DB 361 SNGHTESILSESHSVIWMSSVENSRHSPTGPGRLNGTGGPRECNPSLRHARETPOSY 420
 QY 421 RDSPHSERVVSAMTTPARMSVDPDFTHTSPSPKSPPEMSPPVSSMTVSPMSMAVSPFMBEE 480
 DB 421 RDSPHSERVVSAMTTPARMSVDPDFTHTSPSPKSPPEMSPPVSSMTVSPMSMAVSPFMBEE 480
 QY 481 RPLLLVTPPRLREKKFDHHPQOFSSFHNNPAHDSNSLPASPLRIVEDEEYETTQYEPQAQ 540
 DB 481 RPLLLVTPPRLREKKFDHHPQOFSSFHNNPAHDSNSLPASPLRIVEDEEYETTQYEPQAQ 540
 QY 541 EPVKKLANSRRAKRTKPNGHIANRLEVDNSTSSQSNSESETEDEDERVGEDTFFLGIQNPL 600
 DB 541 EPVKKLANSRRAKRTKPNGHIANRLEVDNSTSSQSNSESETEDEDERVGEDTFFLGIQNPL 600
 QY 601 AASLEATPAFLADSRTPNAGRFSTQBEIQARLSSVIANQDPIAV 645
 DB 601 AASLEATPAFLADSRTPNAGRFSTQBEIQARLSSVIANQDPIAV 645

[illegible]

	Best Local Similarity	100.0%;	Pred. No. 2.3e-204;	Mismatches	0;	Indels	0;	Gaps	0;
	Matches	645;	Conservative	0;					
Qy	1	MSERKEGRGKGKGGKKERGSGKPESAGSQSPALPQLKEMKSQESAAGSKLVLRCTS	60						
Dd	31	MSERKEGRGKGKGGKKERGSGKPESAGSQSPALPQLKEMKSQESAAGSKLVLRCTS	90						
Qy	61	SEYSSSLRFPKFGNGELNRKNKPNQIKIQQPKGSRLRNKASLADSGEYMCKVISKLG	120						
Dd	91	SEYSSSLRFPKFGNGELNRKNKPNQIKIQQPKGSRLRNKASLADSGEYMCKVISKLG	150						
Qy	121	DSASANTIVNESNEIIITGMPEASTEGAVVSSESPIRISVSTEGANTSSTTGTGSHLV	180						
Dd	151	DSASANTIVNESNEIIITGMPEASTEGAVVSSESPIRISVSTEGANTSSTTGTGSHLV	210						
Qy	181	KCAEKETFCVNGGECFWMKDLSNPSRYLCKCNEFTGDRCONVMVASFYKHGLGFMEPA	240						
Dd	211	KCAEKETFCVNGGECFWMKDLSNPSRYLCKCNEFTGDRCONVMVASFYKHGLGFMEPA	270						
Qy	241	EELYQKRVLTIITGICIALLVVGIMCVVAYCTKKQRKLHDLRQSLRSERNMMNIANG	300						
Dd	271	EELYQKRVLTIITGICIALLVVGIMCVVAYCTKKQRKLHDLRQSLRSERNMMNIANG	330						
Qy	301	PHHPNPENPVOLNVQVSNVISSEHIVERAETSFSHTSTAHHSTTTVTPTPSHW	360						
Dd	331	PHHPNPENPVOLNVQVSNVISSEHIVERAETSFSHTSTAHHSTTTVTPTPSHW	390						
Qy	361	SNGTHESIESHSVIWMSSVENSRHSSPTGGPRGLNTGGPRECNFLRHARETPDSY	420						
Dd	391	SNGTHESIESHSVIWMSSVENSRHSSPTGGPRGLNTGGPRECNFLRHARETPDSY	450						
Qy	421	RDSPHSERYVSAMTTPARMSPVDFHTPPSPKSPPPSEMSPVSSMTVSMFMAVPFMEE	480						
Dd	451	RDSPHSERYVSAMTTPARMSPVDFHTPPSPKSPPPSEMSPVSSMTVSMFMAVPFMEE	510						
Qy	481	RPILLVTPPLREKFDHPHQOQSFFHNPDNSLPASPILRIVEDEYEYTOQEYEPQAQ	540						
Dd	511	RPILLVTPPLREKFDHPHQOQSFFHNPDNSLPASPILRIVEDEYEYTOQEYEPQAQ	570						
Qy	541	EPVKCLANSRRAKTKPNGHIANRLEVDNSTSSQSNSESETEDRVGSDTFPLGIQNPL	600						
Dd	571	EPVKCLANSRRAKTKPNGHIANRLEVDNSTSSQSNSESETEDRVGSDTFPLGIQNPL	630						
Qy	601	AASLEATPAFLADSRTPNAGRSTQEEIQARLSSVIANQDPIAV	645						
Dd	631	AASLEATPAFLADSRTPNAGRSTQEEIQARLSSVIANQDPIAV	675						
RESULT	6								
AAAY71172	ID	AAAY71172 standard; protein; 675 AA.							
XX	AC	AAAY71172;							
XX	DT	21-SEP-2000 (first entry)							
XX	DE	Human Heregulin HRG-beta1 protein.							
KW		Heregulin; HRG beta1; human; hair cell; inner-ear-supporting cell;							
KW		activator; HER2 receptor; HER3 receptor; HER-2 oncogene; chromosome 8p;							
KW		hair cell related hearing disorder; ototoxic injury; tissue damage;							
KW		acoustic assault; degenerative hearing loss; balance impairment;							
XX		treatment; surgical injury; physical injury; inner ear disorder.							
OS		Homo sapiens.							
XX	Key	Location/Qualifiers							
FH	Cleavage-site	31..32							
FT	/note=	"Cleavage results in amino terminal fragment of							
FT	HRG-beta1	protein"							
FT	Misc-difference	31							
FT	/label=	Initiator_methionine							
FT	Domain	212..251							

FT	/label=	Growth_factor_domain							
FT	/note=	"HRG-beta-GPD"							
FT	Cleavage-site	255..256							
FT	/note=	"Cleavage results in carboxy terminal fragment of							
FT	HRG-beta1	protein"							
FT	Cleavage-site	261..262							
FT	/note=	"Cleavage results in carboxy terminal fragment of							
FT	HRG-beta1	protein"							
FT	Cleavage-site	276..277							
FT	/note=	"Cleavage results in carboxy terminal fragment of							
FT	HRG-beta1	protein"							
XX	WO2000027426-A1.								
PN	18-MAY-2000.								
PD	28-OCT-1999;	99WO-US025744.							
PF	07-NOV-1998;	98US-0107522P.							
PR	(GETH) GENENTECH INC.								
PA	Gao W;								
XX	Method for inducing hair cell generation and inner-ear-supporting cell growth regeneration and proliferation, useful for treating hearing disorders.								
XX	Disclosure; Fig 2; 141pp; English.</								

XX WO200027426-A1.
XX 18-MAY-2000.
XX 28-OCT-1999; 99WO-US025744.
XX 07-NOV-1998; 98US-0107522P.
XX (GETH) GENENTECH INC.
XX Gao W;
XX WPI; 2000-376313/32.
XX Method for inducing hair cell generation and inner-ear-supporting cell
PT growth regeneration and proliferation, useful for treating hearing
PT disorders.
XX Disclosure; Page; 141pp; English.
XX The patent discloses a method for inducing hair cell generation, or inner
CC -ear-supporting cell growth, regeneration, and/or proliferation, by
CC heregulin (HRG), the ligand for HER2/HER3 dimeric receptors. Heregulin
CC proteins function as activators of HER-2 oncogene and result from
CC alternate splicing of a single gene mapped to chromosome 8p. The two
CC major types, alpha and beta HRG's are based on two variant EGF-like
CC (epidermal growth factor) domains, that differ in their C-terminal ends.
CC This method can be used to increase the number of inner-ear-supporting
CC cells and for treatment of hair cell related hearing disorders and
CC disease states associated with tissue damage, e.g. ototoxic injury,
CC acoustic assault, degenerative hearing loss, balance impairments, damage
CC associated with surgery or physical injury and inner ear disorders
CC related to hair cell dysfunction. The present sequence is the human
CC heregulin ligand, HRG-beta1 protein variant-11. Note: This sequence is
CC not found in the specification and is derived from the HRG-beta1 protein
CC sequence found in Figure 2 (AAV711172)
XX
XX Sequence 675 AA;
Query Match 99.9%; Score 3344; DB 3; Length 675;
Best Local Similarity 99.8%; Pred. No. 3.6e-204;
Matches 644; Conservative 1; Mismatches 0; Indels 0; Gaps 0;
QY 1 MSERKEGRGKGGKKGKSGKPPSAAGSQSPALPPQIKEMKQESAGSKVLVRCETS 60
DB 31 MSERKEGRGKGGKKGKSGKPPSAAGSQSPALPPQIKEMKQESAGSKVLVRCETS 90
QY 61 SEYSLRFKFWKNGELNKNKPNQIKIQKPGKSELINKASLADSGEYMKVSKLGN 120
DB 91 SEYSLRFKFWKNGELNKNKPNQIKIQKPGKSELINKASLADSGEYMKVSKLGN 150
QY 121 DSASANITIVESNEIITGMPASTEGAYVSSSPIRISVSTEGANTSSSTSTSTTCTSHLV 180
DB 151 DSASANITIVESNEIITGMPASTEGAYVSSSPIRISVSTEGANTSSSTSTSTTCTSHLV 210
QY 181 KCAEKEKTCVNGGCFWYKDLNSRSLCKPCNFTGDRCONYMAFYKHLGIEFMEA 240
DB 211 KCAEKEKTCVNGGCFWYKDLNSRSLCKPCNFTGDRCONYMAFYKHLGIEFMEA 270
QY 241 BELYQKRVLTITGICIALLVGIMCVAYCKTKQKQKLDRLQSLRSERNMNIANG 300
DB 271 BELYQKRVLTITGICIALLVGIMCVAYCKTKQKQKLDRLQSLRSERNMNIANG 330
QY 301 PHHPNPPNPNVQNVSKNVISSSEHIVERAEATSFSTSHVTSTAHSHTTQTTPSHW 360
DB 331 PHHPNPPNPNVQNVSKNVISSSEHIVERAEATSFSTSHVTSTAHSHTTQTTPSHW 390
QY 361 SNGHTESILSESHSVTKSVSSVNSHSPSTGGPRGLNGTGGPRCNFLRHARETPDSY 420
DB 391 SNGHTESILSESHSVTKSVSSVNSHSPSTGGPRGLNGTGGPRCNFLRHARETPDSY 450
QY 421 RDSPHSERYVSAMTTTPARMSPVDFHTPSSPKSPPEMSPVSSMTVSPMAVSPFMBEE 480

DB 451 RDSPHSERYVSAMTTTPARMSPVDFHTPSSPKSPPEMSPVSSMTVSPMAVSPFMBEE 510
QY 481 RPLLVTTPRLREKFDHHPQOQSFHFNPAHDSNLSPLRIVEDEEYETQSYEPAQ 540
DB 511 RPLLVTTPRLREKFDHHPQOQSFHFNPAHDSNLSPLRIVEDEEYETQSYEPAQ 570
QY 541 EPVKLANSSRAKRTKPNGHIANRLEVDNSTSSQSSNSESETEDRVEDTFFLGIQNPL 600
DB 571 EPVKLANSSRAKRTKPNGHIANRLEVDNSTSSQSSNSESETEDRVEDTFFLGIQNPL 630
QY 601 AASLEATPAFLADSRTPNAGRFSTQEBEIQARLSSVIANQDPIAV 645
DB 631 AASLEATPAFLADSRTPNAGRFSTQEBEIQARLSSVIANQDPIAV 675
RESULT 10
AAV711189
ID AAV711189 standard; protein; 675 AA.
XX
XX AAV711189;
AC
DT 21-SEP-2000 (first entry)
XX
DE Human Heregulin HRG-beta1 protein variant-12.
XX
KW Heregulin; HRG beta1; human; mutant; mutein; inner-ear-supporting cell;
KW activator; HER2 receptor; HER3 receptor; HER-2 oncogene; chromosome 8p;
KW hair cell related hearing disorder; ototoxic injury; tissue damage;
KW acoustic assault; degenerative hearing loss; balance impairment;
KW treatment; surgical injury; physical injury; inner ear disorder.
XX
OS Homo sapiens.
XX Synthetic.
XX
XX Key
XX Misc-difference 31
XX Location/Qualifiers
FT
FT Misc-difference 227
FT /note= "Wild type Phe replaced with Tyr; This variable
FT site corresponds to position 197, of the HRG-beta1 mature
FT protein, after initiator Met (M31)"
XX
XX WO200027426-A1.
XX 18-MAY-2000.
XX 28-OCT-1999; 99WO-US025744.
XX 07-NOV-1998; 98US-0107522P.
XX (GETH) GENENTECH INC.
XX Gao W;
XX WPI; 2000-376313/32.
XX Method for inducing hair cell generation and inner-ear-supporting cell
PT growth regeneration and proliferation, useful for treating hearing
PT disorders.
XX Disclosure; Page; 141pp; English.
XX The patent discloses a method for inducing hair cell generation, or inner
CC -ear-supporting cell growth, regeneration, and/or proliferation, by
CC heregulin (HRG), the ligand for HER2/HER3 dimeric receptors. Heregulin
CC proteins function as activators of HER-2 oncogene and result from
CC alternate splicing of a single gene mapped to chromosome 8p. The two
CC major types, alpha and beta HRG's are based on two variant EGF-like
CC (epidermal growth factor) domains, that differ in their C-terminal ends.
CC This method can be used to increase the number of inner-ear-supporting
CC cells and for treatment of hair cell related hearing disorders and
CC disease states associated with tissue damage, e.g. ototoxic injury,
CC associated with surgery or physical injury and inner ear disorders
CC related to hair cell dysfunction. The present sequence is the human
CC heregulin ligand, HRG-beta1 protein variant-11. Note: This sequence is
CC not found in the specification and is derived from the HRG-beta1 protein
CC sequence found in Figure 2 (AAV711172)
XX
XX Sequence 675 AA;
Query Match 99.9%; Score 3344; DB 3; Length 675;
Best Local Similarity 99.8%; Pred. No. 3.6e-204;
Matches 644; Conservative 1; Mismatches 0; Indels 0; Gaps 0;
QY 1 MSERKEGRGKGGKKGKSGKPPSAAGSQSPALPPQIKEMKQESAGSKVLVRCETS 60
DB 31 MSERKEGRGKGGKKGKSGKPPSAAGSQSPALPPQIKEMKQESAGSKVLVRCETS 90
QY 61 SEYSLRFKFWKNGELNKNKPNQIKIQKPGKSELINKASLADSGEYMKVSKLGN 120
DB 91 SEYSLRFKFWKNGELNKNKPNQIKIQKPGKSELINKASLADSGEYMKVSKLGN 150
QY 121 DSASANITIVESNEIITGMPASTEGAYVSSSPIRISVSTEGANTSSSTSTSTTCTSHLV 180
DB 151 DSASANITIVESNEIITGMPASTEGAYVSSSPIRISVSTEGANTSSSTSTSTTCTSHLV 210
QY 181 KCAEKEKTCVNGGCFWYKDLNSRSLCKPCNFTGDRCONYMAFYKHLGIEFMEA 240
DB 211 KCAEKEKTCVNGGCFWYKDLNSRSLCKPCNFTGDRCONYMAFYKHLGIEFMEA 270
QY 241 BELYQKRVLTITGICIALLVGIMCVAYCKTKQKQKLDRLQSLRSERNMNIANG 300
DB 271 BELYQKRVLTITGICIALLVGIMCVAYCKTKQKQKLDRLQSLRSERNMNIANG 330
QY 301 PHHPNPPNPNVQNVSKNVISSSEHIVERAEATSFSTSHVTSTAHSHTTQTTPSHW 360
DB 331 PHHPNPPNPNVQNVSKNVISSSEHIVERAEATSFSTSHVTSTAHSHTTQTTPSHW 390
QY 361 SNGHTESILSESHSVTKSVSSVNSHSPSTGGPRGLNGTGGPRCNFLRHARETPDSY 420
DB 391 SNGHTESILSESHSVTKSVSSVNSHSPSTGGPRGLNGTGGPRCNFLRHARETPDSY 450
QY 421 RDSPHSERYVSAMTTTPARMSPVDFHTPSSPKSPPEMSPVSSMTVSPMAVSPFMBEE 480

CC acoustic assault, degenerative hearing loss, balance impairments, damage
CC associated with surgery or physical injury and inner ear disorders
CC related to hair cell dysfunction. The present sequence is the human
CC heregulin ligand, HRG-beta1 protein variant-12. Note: This sequence is
CC not found in the specification and is derived from the HRG-beta1 protein
CC sequence found in Figure 2 (AAY711172)

XX SQ Sequence 675 AA;

Query Match 99.9%; Score 3344; DB 3; Length 675;
Best Local Similarity 99.8%; Pred. No. 3.6e-204; Indels 0; Gaps 0;
Matches 644; Conservative 1; Mismatches 0;

QY 1 MSERKEGRGKGGKXKRGSGKKPESAAAGSQSPALPPQKEMKQESAAAGSKVLRCETS 60
DB 31 MSERKEGRGKGGKXKRGSGKKPESAAAGSQSPALPPQKEMKQESAAAGSKVLRCETS 90
QY 61 SEYSSLRPFKFNKGNELRNKPNQIKIQKPKGKSELINKASLADSGEYMKVSKLGN 120
DB 91 SEYSSLRPFKFNKGNELRNKPNQIKIQKPKGKSELINKASLADSGEYMKVSKLGN 150
QY 121 DSASANITIVESNEIITGMPASTEGAYVSSSEPIRISVSTEGANTSSSTSTTGTSHLV 180
DB 151 DSASANITIVESNEIITGMPASTEGAYVSSSEPIRISVSTEGANTSSSTSTTGTSHLV 210
QY 181 KCAEKEKTFVNGGECFVWKDLSNPSRYLCKPNEFTGDRCCQNYVMASFYKHLGIEFMEA 240
DB 211 KCAEKEKTFVNGGECFVWKDLSNPSRYLCKPNEFTGDRCCQNYVMASFYKHLGIEFMEA 270
QY 241 EELYQKRVLTITGICITALLVGMICVAVCYKTKQKQKLDHRLQSLRERNMMNIANG 300
DB 271 EELYQKRVLTITGICITALLVGMICVAVCYKTKQKQKLDHRLQSLRERNMMNIANG 330
QY 301 PHPNPPEPVQVNVQVSKNVISSEHIVERAETSFSHTYSTAHSTTTTQTPSHSW 360
DB 331 PHPNPPEPVQVNVQVSKNVISSEHIVERAETSFSHTYSTAHSTTTTQTPSHSW 390
QY 361 SNGHTESILSESHSVIVMSSVENSRSPTGGPRGLNGTGGPRECNFLRHARETPDSY 420
DB 391 SNGHTESILSESHSVIVMSSVENSRSPTGGPRGLNGTGGPRECNFLRHARETPDSY 450
QY 421 RDSPHSERVYSAATTTPARMSVDFTPPSPKSPSPSPSPSPSPSPSPSPSPSPSPSP 480
DB 451 RDSPHSERVYSAATTTPARMSVDFTPPSPKSPSPSPSPSPSPSPSPSPSPSPSPSP 510
QY 481 RPLLVTPRLREKKEFDHPQPFSSPHHPADNSLPSPLRIVEDEYETTOYEPAQ 540
DB 511 RPLLVTPRLREKKEFDHPQPFSSPHHPADNSLPSPLRIVEDEYETTOYEPAQ 570
QY 541 EPVKKLANGRRARRTKPNGHIANRLEVDNSTSQSSNSESETEDEVRVGDTPFLGIONPL 600
DB 571 EPVKKLANGRRARRTKPNGHIANRLEVDNSTSQSSNSESETEDEVRVGDTPFLGIONPL 630
QY 601 AASLEATPAFLADSTNTPAGRPSTOEIQAARLSSVIANQDPIAV 645
DB 631 AASLEATPAFLADSTNTPAGRPSTOEIQAARLSSVIANQDPIAV 675

RESULT 11

AAY711191
ID AAY711191 standard; protein; 675 AA.

XX AC AAY711191;

XX DT 21-SEP-2000 (first entry)

XX DE Human Heregulin HRG-beta1 protein variant-14.

XX KW Heregulin; HRG beta1; human; mutant; mutein; inner-ear-supporting cell;
KW activator; HER2 receptor; HER3 receptor; HER-2 oncogene; chromosome 8p;
KW hair cell related hearing disorder; ototoxic injury; tissue damage;
KW acoustic assault; degenerative hearing loss; balance impairment;
KW treatment; surgical injury; physical injury; inner ear disorder.

XX OS Homo sapiens.
OS Synthetic.

XX FH Key Location/Qualifiers

FT Misc-difference 31 /Label= Initiator_methionine

FT Misc-difference 230

FT FT /note= "Wild type Lys replaced with Arg; This variable site corresponds to position 200, of the HRG-beta1 mature protein, after initiator Met (M31)"

XX PN WO200027426-A1.

XX PD 18-MAY-2000.

XX PF 28-OCT-1999; 99WO-US025744.

XX PR 07-NOV-1998; 98US-0107522P.

XX PA (GETH) GENENTECH INC.

XX PI Gao W;

XX DR WPI; 2000-376313/32.

XX Method for inducing hair cell generation and inner-ear-supporting cell growth regeneration and proliferation, useful for treating hearing disorders.
XX Disclosure; Page; 141pp; English.
XX The patent discloses a method for inducing hair cell generation, or inner-ear-supporting cell growth, regeneration, and/or proliferation, by heregulins (HRG), the ligand for HER2/HER3 dimeric receptors. Heregulin proteins function as activators of HER-2 oncogene and result from alternate splicing of a single gene mapped to chromosome 8p. The two major types, alpha and beta HRG's are based on two variant EGF-like (epidermal growth factor) domains, that differ in their C-terminal ends. This method can be used to increase the number of inner-ear-supporting cells and for treatment of hair cell related hearing disorders and disease states associated with tissue damage, e.g. ototoxic injury, acoustic assault, degenerative hearing loss, balance impairments, damage associated with surgery or physical injury and inner ear disorders related to hair cell dysfunction. The present sequence is the human heregulin ligand, HRG-beta1 protein variant-14. Note: This sequence is not found in the specification and is derived from the HRG-beta1 protein sequence found in Figure 2 (AAY711172)

XX SQ Sequence 675 AA;

Query Match 99.9%; Score 3344; DB 3; Length 675;
Best Local Similarity 99.8%; Pred. No. 3.6e-204; Indels 0; Gaps 0;
Matches 644; Conservative 1; Mismatches 0;

QY 1 MSERKEGRGKGGKXKRGSGKKPESAAAGSQSPALPPQKEMKQESAAAGSKVLRCETS 60
DB 31 MSERKEGRGKGGKXKRGSGKKPESAAAGSQSPALPPQKEMKQESAAAGSKVLRCETS 90

QY 61 SEYSSLRPFKFNKGNELRNKPNQIKIQKPKGKSELINKASLADSGEYMKVSKLGN 120
DB 91 SEYSSLRPFKFNKGNELRNKPNQIKIQKPKGKSELINKASLADSGEYMKVSKLGN 150

QY 121 DSASANITIVESNEIITGMPASTEGAYVSSSEPIRISVSTEGANTSSSTSTTGTSHLV 180
DB 151 DSASANITIVESNEIITGMPASTEGAYVSSSEPIRISVSTEGANTSSSTSTTGTSHLV 210

QY 181 KCAEKEKTFVNGGECFVWKDLSNPSRYLCKPNEFTGDRCCQNYVMASFYKHLGIEFMEA 240
DB 211 KCAEKEKTFVNGGECFVWKDLSNPSRYLCKPNEFTGDRCCQNYVMASFYKHLGIEFMEA 270

QY 241 EELYQKRVLTITGICITALLVGMICVAVCYKTKQKQKLDHRLQSLRERNMMNIANG 300
DB 271 EELYQKRVLTITGICITALLVGMICVAVCYKTKQKQKLDHRLQSLRERNMMNIANG 330

Db 271 EELYQKRVLTITGICALLVVGIMCVVAYCKTKQKQKLDRLRQSLRSENNMMNIANG 330
 QY 301 PHPNPPENQVNVQVSKNVLSSHHIVERAEFTSFSTHYTSTAHHSTTTTTPSHSW 360
 Db 331 PHPNPPENQVNVQVSKNVLSSHHIVERAEFTSFSTHYTSTAHHSTTTTTPSHSW 390
 QY 361 SNGHTESILSESHSVIMSSVENSRRHSPTGGPRGLNGTGGPRECNFLRHARETPDSY 420
 Db 391 SNGHTESILSESHSVIMSSVENSRRHSPTGGPRGLNGTGGPRECNFLRHARETPDSY 450
 QY 421 RDSPHSERVYSAMTTTPARMSVDFTPTSPKSPPEMSPPVSSMTVMSPMAVSPPEEE 480
 Db 451 RDSPHSERVYSAMTTTPARMSVDFTPTSPKSPPEMSPPVSSMTVMSPMAVSPPEEE 510
 QY 481 RPLLLVTPPLREKKFDHHPQOQSSFFHNPANDNSLPASPLRIVEDEEYETTOYEPAQ 540
 Db 511 RPLLLVTPPLREKKFDHHPQOQSSFFHNPANDNSLPASPLRIVEDEEYETTOYEPAQ 570
 QY 541 EPVKLANRRAKRTKPNGHIANRLEVDNNTSSQSSNSETEDEVRGDTTFLGIQNPL 600
 Db 571 EPVKLANRRAKRTKPNGHIANRLEVDNNTSSQSSNSETEDEVRGDTTFLGIQNPL 630
 QY 601 AASLEATPAFLADSRTPAGRFSTQEEIQARLSSVIANQDPIAV 645
 Db 631 AASLEATPAFLADSRTPAGRFSTQEEIQARLSSVIANQDPIAV 675

RESULT 12
 AAY71182
 ID AAY71182 standard; protein; 675 AA.
 XX AC AAY71182;
 DT 21-SEP-2000 (first entry)
 XX DE Human Heregulin HRG-beta1 protein variant-5.
 KW Heregulin; HRG beta1; human; mutant; mutein; inner-ear-supporting cell;
 KW activator; HER2 receptor; HER3 receptor; HER-2 oncogene; chromosome 8p;
 KW hair cell related hearing disorder; ototoxic injury; tissue damage;
 KW acoustic assault; degenerative hearing loss; balance impairment;
 KW treatment; surgical injury; physical injury; inner ear disorder.
 XX OS Homo sapiens.
 OS Synthetic.
 XX PH Key Location/Qualifiers
 FT Misc-difference 31 /label= Initiator_methionine
 FT Misc-difference 213
 FT FT notes "Wild type Ala replaced with Gly; This variable
 FT site corresponds to position 183, of the HRG-beta1 mature
 FT protein, after initiator Met (M31)"
 XX WO200027426-A1.
 PN 18-MAY-2000.
 XX PD 28-OCT-1999; 99WO-US025744.
 XX PF 07-NOV-1998; 98US-0107522P.
 XX PR (GETH) GENENTECH INC.
 XX PA Gao W;
 XX PI WPI; 2000-376313/32.
 XX DR Method for inducing hair cell generation and inner-ear-supporting cell
 PT growth regeneration and proliferation, useful for treating hearing
 PT disorders.
 XX PS Disclosure; Page; 141pp; English.

XX The patent discloses a method for inducing hair cell generation, or inner
 CC -ear-supporting cell growth, regeneration, and/or proliferation, by
 CC heregulin (HRG), the ligand for HER2/HER3 dimeric receptors. Heregulin
 CC proteins function as activators of HER-2 oncogene and result from
 CC alternate splicing of a single gene mapped to chromosome 8p. The two
 CC major types, alpha and beta HRG's are based on two variant SGP-like
 CC (epidermal growth factor) domains, that differ in their C-terminal ends.
 CC This method can be used to increase the number of inner-ear-supporting
 CC cells and for treatment of hair cell related hearing disorders and
 CC disease states associated with tissue damage, e.g. ototoxic injury,
 CC acoustic assault, degenerative hearing loss, balance impairments, damage
 CC associated with surgery or physical injury and inner ear disorders
 CC related to hair cell dysfunction. The present sequence is the human
 CC heregulin ligand, HRG-beta1 protein variant-5. Note: This sequence is not
 CC found in the specification and is derived from the HRG-beta1 protein
 CC sequence found in Figure 2 (AAY71172)
 XX
 SQ Sequence 675 AA;

Query Match 99.9%; Score 3343; DB 3; Length 675;
 Best Local Similarity 99.8%; Pred. No. 4.le-204;
 Matches 644; Conservative 0; Mismatches 1; Indels 0; Gaps 0;
 QY 1 MSERKEGRGKGGKKGKSGKSPESAGSOSPALPOLKEMKSOESAGSKVLRCETS 60
 Db 31 MSERKEGRGKGGKKGKSGKSPESAGSOSPALPOLKEMKSOESAGSKVLRCETS 90
 QY 61 SEYSSLRFPKFGKNGNELNKNKPNQIKIQKPGKSELINKASLADSGEYCKVISKIGN 120
 Db 91 SEYSSLRFPKFGKNGNELNKNKPNQIKIQKPGKSELINKASLADSGEYCKVISKIGN 150
 QY 121 DSANITIVNESNIIITGMPASTEGAYVSSSPTRISVSTEGANTSSSTSTTGTSHLV 180
 Db 151 DSANITIVNESNIIITGMPASTEGAYVSSSPTRISVSTEGANTSSSTSTTGTSHLV 210
 QY 181 KCAKEKTEFCVNGGECFMVKDLSNPRLCKPNEFTGDRCONTVMASFYKHLGIEPMEA 240
 Db 211 KCGEKEKTEFCVNGGECFMVKDLSNPRLCKPNEFTGDRCONTVMASFYKHLGIEPMEA 270
 QY 241 EELYQKRVLTITGICALLVVGIMCVVAYCKTKQKQKLDRLRQSLRSENNMMNIANG 300
 Db 271 EELYQKRVLTITGICALLVVGIMCVVAYCKTKQKQKLDRLRQSLRSENNMMNIANG 330
 QY 301 PHPNPPENQVNVQVSKNVLSSHHIVERAEFTSFSTHYTSTAHHSTTTTTPSHSW 360
 Db 331 PHPNPPENQVNVQVSKNVLSSHHIVERAEFTSFSTHYTSTAHHSTTTTTPSHSW 390
 QY 361 SNGHTESILSESHSVIMSSVENSRRHSPTGGPRGLNGTGGPRECNFLRHARETPDSY 420
 Db 391 SNGHTESILSESHSVIMSSVENSRRHSPTGGPRGLNGTGGPRECNFLRHARETPDSY 450
 QY 421 RDSPHSERVYSAMTTTPARMSVDFTPTSPKSPPEMSPPVSSMTVMSPMAVSPPEEE 480
 Db 451 RDSPHSERVYSAMTTTPARMSVDFTPTSPKSPPEMSPPVSSMTVMSPMAVSPPEEE 510
 QY 481 RPLLLVTPPLREKKFDHHPQOQSSFFHNPANDNSLPASPLRIVEDEEYETTOYEPAQ 540
 Db 511 RPLLLVTPPLREKKFDHHPQOQSSFFHNPANDNSLPASPLRIVEDEEYETTOYEPAQ 570
 QY 541 EPVKLANRRAKRTKPNGHIANRLEVDNNTSSQSSNSETEDEVRGDTTFLGIQNPL 600
 Db 571 EPVKLANRRAKRTKPNGHIANRLEVDNNTSSQSSNSETEDEVRGDTTFLGIQNPL 630
 QY 601 AASLEATPAFLADSRTPAGRFSTQEEIQARLSSVIANQDPIAV 645
 Db 631 AASLEATPAFLADSRTPAGRFSTQEEIQARLSSVIANQDPIAV 675

RESULT 13
 AAY71203
 ID AAY71203 standard; protein; 675 AA.
 XX

PA (GETH) GENENTECH INC.
XX Gao W;
PI WPI; 2000-376313/32.
XX
PT Method for inducing hair cell generation and inner-ear-supporting cell
PT growth regeneration and proliferation, useful for treating hearing
PT disorders.
XX
PS Disclosure; Page; 141pp; English.
XX
CC The patent discloses a method for inducing hair cell generation, or inner
CC -ear-supporting cell growth, regeneration, and/or proliferation, by
CC heregulin (HRG), the ligand for HER2/HER3 dimeric receptors. Heregulin
CC proteins function as activators of HER-2 oncogene and result from
CC alternate splicing of a single gene mapped to chromosome 8p. The two
CC major types, alpha and beta HRG's are based on two variant EGF-like
CC (epidermal growth factor) domains, that differ in their C-terminal ends.
CC This method can be used to increase the number of inner-ear-supporting
CC cells and for treatment of hair cell related hearing disorders and
CC disease states associated with tissue damage, e.g. ototoxic injury,
CC acoustic assault, degenerative hearing loss, balance impairments, damage
CC associated with surgery or physical injury and inner ear disorders
CC related to hair cell dysfunction. The present sequence is the human
CC heregulin ligand, HRG-beta1 protein variant-17. Note: This sequence is
CC not found in the specification and is derived from the HRG-beta1 protein
CC sequence found in Figure 2 (AA71172)
XX
SQ Sequence 675 AA;

Query Match 99.9%; Score 3343; DB 3; Length 675;
Best Local Similarity 99.8%; Pred. No. 4.1e-204;
Matches 644; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

QY 1 MSERKEGRGKGKKGKESGKPPSAAGSQSPALPPQLKEMKQESAGSKVLRCETS 60
DB |||||
DB 31 MSERKEGRGKGKKGKESGKPPSAAGSQSPALPPQLKEMKQESAGSKVLRCETS 90
QY 61 SEYSSLRFFWFKNGELNKNPQNIKIQQKPKSELINKASLADSGEYMKVSKLGN 120
DB |||||
DB 91 SEYSSLRFFWFKNGELNKNPQNIKIQQKPKSELINKASLADSGEYMKVSKLGN 150
QY 121 DSASANITIVESNEIITGMPASTEGAYVSSSPIRISVSTEGANTSSSTSTTGTGSHLV 180
DB |||||
DB 151 DSASANITIVESNEIITGMPASTEGAYVSSSPIRISVSTEGANTSSSTSTTGTGSHLV 210
QY 181 KCAEKEKTCVNGGECFVMDLSNPSRYLCKPCNEFTGDRQCNVYVWASFYKHLGIEFMEA 240
DB |||||
DB 211 KCAEKEKTCVNGGECFVMDLSNPSRYLCKPCNEFTGDRQCNVYVWASFYKHLGIEFMEA 270
QY 241 EELYQKRVLTITGICITALLVGMCMVAVCKTKQKQKLDRLQSLRSERNMNIANG 300
DB |||||
DB 271 EELYQKRVLTITGICITALLVGMCMVAVCKTKQKQKLDRLQSLRSERNMNIANG 330
QY 301 PPHPNPPPNVQLVQYVSKNIVSESHIVERAEATSFSTSHYSTAHSTTTVTPSHSW 360
DB |||||
DB 331 PPHPNPPPNVQLVQYVSKNIVSESHIVERAEATSFSTSHYSTAHSTTTVTPSHSW 390
QY 361 SNGHTESILSESHSVTMSVSNRHSPTGPGRLNGTGPGRCNGLRHARETPDSY 420
DB |||||
DB 391 SNGHTESILSESHSVTMSVSNRHSPTGPGRLNGTGPGRCNGLRHARETPDSY 450
QY 421 RSPHSERVVSAMTPARNSPVDFHTPPSPKPPSPSPVSSMTVSPMSMAVSPFMBEE 480
DB |||||
DB 451 RSPHSERVVSAMTPARNSPVDFHTPPSPKPPSPSPVSSMTVSPMSMAVSPFMBEE 510
QY 481 RPLLVTPRLREKFDHHPQFSSFHNPADNSLPASPLRIVEDEYEYETQYVEPAQ 540
DB |||||
DB 511 RPLLVTPRLREKFDHHPQFSSFHNPADNSLPASPLRIVEDEYEYETQYVEPAQ 570
QY 541 EPVKKLANRRAKRTKPNGHIANRLEVDNSTSSQSSNSESETEDRVEDTFFLGIONPL 600
DB |||||

DB 571 EPVKKLANRRAKRTKPNGHIANRLEVDNSTSSQSSNSESETEDRVEDTFFLGIONPL 630
QY 601 AASLEATPAFLADSRTPNAGFSTQEEIOARLSSVIANODPIAV 645
DB |||||
DB 631 AASLEATPAFLADSRTPNAGFSTQEEIOARLSSVIANODPIAV 675

RESULT 15
AA71180
ID AAY71180 standard; protein; 675 AA.
XX
AC AAY71180;
DT 21-SEP-2000 (first entry)
XX
DE Human Heregulin HRG-beta1 protein variant-3.
XX
KW Heregulin; HRG beta1; human; mutant; mutein; inner-ear-supporting cell;
KW activator; HER2 receptor; HER3 receptor; HER-2 oncogene; chromosome 8p;
KW hair cell related hearing disorder; ototoxic injury; tissue damage;
KW acoustic assault; degenerative hearing loss; balance impairment;
KW treatment; surgical injury; physical injury; inner ear disorder.
XX
OS Homo sapiens.
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Misc-difference 31 /label= Initiator_methionine
FT Misc-difference 210
FT /label= Gln, Ile, Glu
FT /note= "This variable site corresponds to position 180 of
FT the HRG-beta1 mature protein, after initiator Met (M31)"
XX
PN WO200027426-A1.
XX
PD 18-MAY-2000.
XX
PF 28-OCT-1999; 99WO-US025744.
XX
PR 07-NOV-1998; 98US-0107522P.
XX
PA (GETH) GENENTECH INC.
XX
Gao W;
XX
WPI; 2000-376313/32.
XX
PT Method for inducing hair cell generation and inner-ear-supporting cell
PT growth regeneration and proliferation, useful for treating hearing
PT disorders.
XX
PS Disclosure; Page; 141pp; English.
XX
CC The patent discloses a method for inducing hair cell generation, or inner
CC -ear-supporting cell growth, regeneration, and/or proliferation, by
CC heregulin (HRG), the ligand for HER2/HER3 dimeric receptors. Heregulin
CC proteins function as activators of HER-2 oncogene and result from
CC alternate splicing of a single gene mapped to chromosome 8p. The two
CC major types, alpha and beta HRG's are based on two variant EGF-like
CC (epidermal growth factor) domains, that differ in their C-terminal ends.
CC This method can be used to increase the number of inner-ear-supporting
CC cells and for treatment of hair cell related hearing disorders and
CC disease states associated with tissue damage, e.g. ototoxic injury,
CC acoustic assault, degenerative hearing loss, balance impairments, damage
CC associated with surgery or physical injury and inner ear disorders
CC related to hair cell dysfunction. The present sequence is the human
CC heregulin ligand, HRG-beta1 protein variant-3. Note: This sequence is not
CC found in the specification and is derived from the HRG-beta1 protein
CC sequence found in Figure 2 (AA71172)
XX
SQ Sequence 675 AA;

Query Match	99.9%	Score 3342;	DB 3;	Length 675;
Best Local Similarity	99.8%	Pred. No. 4.8e-204;		
Matches 644;	Conservative 0;	Mismatches 1;	Indels 0;	Gaps 0;
QY	1	MSREKRGKGGKXKRGSGKKDPESAAGSQSPALPPQLKEMKSOESAAGSKVLVRCSTS	60	
DB	31	MSREKRGKGGKXKRGSGKKDPESAAGSQSPALPPQLKEMKSOESAAGSKVLVRCSTS	90	
QY	61	SEYSSLRKFWKNGNELNRKNKPNQIKIQQPKGSELNRINKASLADSGYMKCVLSKLG	120	
DB	91	SEYSSLRKFWKNGNELNRKNKPNQIKIQQPKGSELNRINKASLADSGYMKCVLSKLG	150	
QY	121	DSASANIITIVESNEIITGMPASTEGAVVSSSEPIRISVSTEGANTSSSSTSTTTGTSHLV	180	
DB	151	DSASANIITIVESNEIITGMPASTEGAVVSSSEPIRISVSTEGANTSSSSTSTTTGTSHLX	210	
QY	181	KCAEKXKTFVNGGECFMVKDLSNPRLYLCPCNEFTGDRCONYVNASFYKHLGIEFMEA	240	
DB	211	KCAEKXKTFVNGGECFMVKDLSNPRLYLCPCNEFTGDRCONYVNASFYKHLGIEFMEA	270	
QY	241	BEYQKRVLTITGICIALLVGIMCVAYCKTKQKKLHDLRQSLRSERNMMNIANG	300	
DB	271	BEYQKRVLTITGICIALLVGIMCVAYCKTKQKKLHDLRQSLRSERNMMNIANG	330	
QY	301	PHPNPPPENQVLNQYVSKNVISSSEHIVERAFTSFSTSHYTSTTAHSTTTVTQTPSHW	360	
DB	331	PHPNPPPENQVLNQYVSKNVISSSEHIVERAFTSFSTSHYTSTTAHSTTTVTQTPSHW	390	
QY	361	SNCHTESILSSHSVIUMSSVENSRRHSPGGRGLNGTGGPRECNFLRHARETTPQSY	420	
DB	391	SNCHTESILSSHSVIUMSSVENSRRHSPGGRGLNGTGGPRECNFLRHARETTPQSY	450	
QY	421	RDSPHSERYVSAMTTPARMSVPDHTPTSSPKSPPEMSPPVSSMTVSMPSMAVSPFMBEE	480	
DB	451	RDSPHSERYVSAMTTPARMSVPDHTPTSSPKSPPEMSPPVSSMTVSMPSMAVSPFMBEE	510	
QY	481	REPLLVTTPRLREKKFDHPHQPFSSFHNPANHSNLSPLRIVDEDEYETQYEPAQ	540	
DB	511	REPLLVTTPRLREKKFDHPHQPFSSFHNPANHSNLSPLRIVDEDEYETQYEPAQ	570	
QY	541	EPVKLLANSRAKRTKPNGHIANLEVDNSTSQSSNSESETERDVGDDTFFLGIQNPL	600	
DB	571	EPVKLLANSRAKRTKPNGHIANLEVDNSTSQSSNSESETERDVGDDTFFLGIQNPL	630	
QY	601	AASLEATPAFLIASRTNPACRFQTOBEIOARLSSVIANODPIAV	645	
DB	631	AASLEATPAFLIASRTNPACRFQTOBEIOARLSSVIANODPIAV	675	

This Page Blank (uspto)

GenCore version 5.1.6
Copyright (c) 1993 - 2005 Compugen Ltd.

OM protein - protein search, using sw model

Run on: April 12, 2005, 14:27:47 ; Search time 43 Seconds
(without alignments)
1119.736 Million cell updates/sec

Title: US-10-082-747A-93

Perfect score: 3347

Sequence: 1 MSERKEGRKGKGGKRRGS.....QEEIQARLSSVIANQPIAV 645

Scoring table: BLOSUM62

Gapop 10.0 , Gapext 0.5

Searched: 513545 seqs, 74649064 residues

Total number of hits satisfying chosen parameters: 513545

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%

Maximum Match 100%

Listing first 45 summaries

Database : Issued Patents AA:*

- 1: /cgn2_6/prodata/1/iaa/5A COMB.pep:**
- 2: /cgn2_6/prodata/1/iaa/5B COMB.pep:**
- 3: /cgn2_6/prodata/1/iaa/6A COMB.pep:**
- 4: /cgn2_6/prodata/1/iaa/6B COMB.pep:**
- 5: /cgn2_6/prodata/1/iaa/PCUS COMB.pep:**
- 6: /cgn2_6/prodata/1/iaa/backfilesi.pep:**

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	ID	Description
1	3347	100.0	645	1	US-07-847-743B-27
2	3347	100.0	645	1	US-08-456-201-27
3	3347	100.0	645	1	US-08-428-926-4
4	3347	100.0	645	1	US-08-428-927-4
5	3347	100.0	645	1	US-08-428-298-4
6	3347	100.0	645	1	US-08-339-517-4
7	3347	100.0	645	2	US-08-456-241-27
8	3347	100.0	645	3	US-09-020-880-93
9	3347	100.0	645	3	US-09-101-544-93
10	3347	100.0	645	4	US-09-097-681-3
11	3347	100.0	645	5	PCT-US92-04295A-27
12	3347	100.0	732	1	US-07-847-743B-9
13	3347	100.0	732	1	US-08-456-201-9
14	3347	100.0	732	2	US-08-456-241-9
15	3347	100.0	732	5	PCT-US92-04295A-9
16	3343	99.9	645	3	US-08-753-007A-10
17	3343	99.9	645	3	US-09-398-496-10
18	3332.5	99.6	646	4	US-08-467-602-270
19	3332.5	99.6	646	4	US-08-411-295F-196
20	3311	98.9	669	4	US-08-467-602-273
21	3311	98.9	669	4	US-08-411-295F-199
22	3299	98.6	693	4	US-08-467-602-271
23	3299	98.6	693	4	US-08-411-295F-197
24	3286	98.2	637	4	US-08-467-602-258
25	3286	98.2	637	4	US-08-411-295F-184
26	3284	98.1	637	1	US-07-847-743B-28
27	3284	98.1	637	1	US-08-456-201-28

28	3284	98.1	637	2	US-08-456-241-28	Sequence 28, Appl
29	3284	98.1	637	5	PCT-US92-04295A-28	Sequence 28, Appl
30	3277.5	97.9	716	4	US-08-467-602-274	Sequence 274, App
31	3277.5	97.9	716	4	US-08-411-295F-200	Sequence 200, App
32	3264.5	97.5	660	4	US-08-467-602-264	Sequence 264, App
33	3264.5	97.5	660	4	US-08-411-295F-190	Sequence 190, App
34	3252.5	97.2	684	4	US-08-467-602-259	Sequence 259, App
35	3252.5	97.2	684	4	US-08-411-295F-185	Sequence 185, App
36	3239	96.8	649	4	US-08-467-602-267	Sequence 267, App
37	3239	96.8	649	4	US-08-411-295F-193	Sequence 193, App
38	3231	96.5	707	4	US-08-467-602-262	Sequence 262, App
39	3231	96.5	707	4	US-08-411-295F-188	Sequence 188, App
40	3205.5	95.8	696	4	US-08-467-602-268	Sequence 268, App
41	3205.5	95.8	696	4	US-08-411-295F-194	Sequence 194, App
42	3198.5	95.6	640	4	US-08-467-602-256	Sequence 256, App
43	3198.5	95.6	640	4	US-08-411-295F-182	Sequence 182, App
44	3198	95.5	895	4	US-08-467-602-354	Sequence 354, App
45	3198	95.5	895	4	US-08-411-295F-280	Sequence 280, App

ALIGNMENTS

RESULT 1
US-07-847-743B-27
; Sequence 27, Application US/07847743B
; Patent No. 5367060
; GENERAL INFORMATION:
; APPLICANT: Genentech, Inc.
; TITLE OF INVENTION: Structure, Production and Use of
; TITLE OF INVENTION: Heregulin
; NUMBER OF SEQUENCES: 30
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Genentech, Inc.
; STREET: 460 Point San Bruno Blvd
; CITY: South San Francisco
; STATE: California
; COUNTRY: USA
; ZIP: 94080
; COMPUTER READABLE FORM:
; MEDIUM TYPE: 5.25 inch, 360 Kb floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: patin (Genentech)
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/07/847,743B
; FILING DATE: 19920306
; CLASSIFICATION: 424
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: 07/705256
; FILING DATE: 24-May-1991
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: 07/765212
; FILING DATE: 25-Sep-1991
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: 07/790801
; FILING DATE: 08-No. 5367060-1991
; ATTORNEY/AGENT INFORMATION:
; NAME: Hensley, Max D.
; REGISTRATION NUMBER: 27,043
; REFERENCE/DOCKET NUMBER: 712P3
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: 415/266-1489
; TELEFAX: 415/952-9881
; TELEX: 910/371-7168
; INFORMATION FOR SEQ ID NO: 27:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 645 amino acids
; TYPE: AMINO ACID
; TOPOLOGY: linear
US-07-847-743B-27

Query Match 100.0%; Score 3347; DB 1; Length 645;

Best Local Similarity 100.0%; Pred. No. 1.3e-244;
Matches 645; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MSERKEGRGKGKGGKGGKPPESAAAGSQSPALPOLKEMKQESAAAGSKLVLRCTS 60
DB 1 MSERKEGRGKGKGGKGGKGGKPPESAAAGSQSPALPOLKEMKQESAAAGSKLVLRCTS 60

QY 61 SEYSSLRFFKFWKNGNELNKNPQNIKIQQKPKSELINKASLADSGEYMKVSKLGN 120
DB 61 SEYSSLRFFKFWKNGNELNKNPQNIKIQQKPKSELINKASLADSGEYMKVSKLGN 120

QY 121 DSANITIVESNEIITGMPASTEGAYVSSSPRISVSTEGANTSSSTSTTTGTSHLV 180
DB 121 DSANITIVESNEIITGMPASTEGAYVSSSPRISVSTEGANTSSSTSTTTGTSHLV 180

QY 181 KCAEKEKTCVNGGECFVKDLSNPRLKCPNEFTGDRCONVYMASFYKHLGIEFMEA 240
DB 181 KCAEKEKTCVNGGECFVKDLSNPRLKCPNEFTGDRCONVYMASFYKHLGIEFMEA 240

QY 241 EELYQKRVLTITGICALLVVGIMCVAYCKTKQKSELINKASLADSGEYMKVSKLGN 300
DB 241 EELYQKRVLTITGICALLVVGIMCVAYCKTKQKSELINKASLADSGEYMKVSKLGN 300

QY 301 PHHPNPPENVOLVNOYVSKNVISSHIVREAEATSFSTSHYTTAHHSSTTTTQPSHW 360
DB 301 PHHPNPPENVOLVNOYVSKNVISSHIVREAEATSFSTSHYTTAHHSSTTTTQPSHW 360

QY 361 SNGHTESILSESHSVIWMSSVNSRHSSPTGGPRGLNGTGPPRECNSFLRHARETDP 420
DB 361 SNGHTESILSESHSVIWMSSVNSRHSSPTGGPRGLNGTGPPRECNSFLRHARETDP 420

QY 421 RDSPHSERVVSAMTTPARMSPVDFHTPSPKPPSEMSPVSSMTVMPMAVSPFMBEE 480
DB 421 RDSPHSERVVSAMTTPARMSPVDFHTPSPKPPSEMSPVSSMTVMPMAVSPFMBEE 480

QY 481 RPLLLVTPRLREKFKDHPHQFSSPHHPNPAHDSNLSPLRIVEDEEYETTOEYEP 540
DB 481 RPLLLVTPRLREKFKDHPHQFSSPHHPNPAHDSNLSPLRIVEDEEYETTOEYEP 540

QY 541 EPVKKLANSRRAKTKPNGHIANRLEVDNSTSSQSNSESETEDEVRGDDTFFLGIQ 600
DB 541 EPVKKLANSRRAKTKPNGHIANRLEVDNSTSSQSNSESETEDEVRGDDTFFLGIQ 600

RESULT 2

US-08-456-201-27
Sequence 27, Application US/08456201
Patent No. 5641869

GENERAL INFORMATION:
APPLICANT: Vandlen, Richard L.,
APPLICANT: Holmes, William E.
TITLE OF INVENTION: Structure, Production and Use of
TITLE OF INVENTION: Heregulin 2 Ligands
NUMBER OF SEQUENCES: 30

CORRESPONDENCE ADDRESS:
ADDRESSEE: Genentech, Inc.
STREET: 460 Point San Bruno Blvd
CITY: South San Francisco
STATE: California
COUNTRY: USA
ZIP: 94080

COMPUTER READABLE FORM:
MEDIUM TYPE: 5.25 inch, 360 Kb floppy disk
COMPUTER: IBM PC compatible
OPERATING SYSTEM: PC-DOS/MS-DOS
SOFTWARE: Patin (Genentech)
CURRENT APPLICATION DATA:
APPLICATION NUMBER: US/08/456,201
FILING DATE:

CLASSIFICATION: 530
PRIOR APPLICATION DATA:
APPLICATION NUMBER: US/08/126,145
FILING DATE:
APPLICATION NUMBER: 07/880,917
PRIOR APPLICATION DATA:
APPLICATION NUMBER: 07/705256
PRIOR APPLICATION DATA:
APPLICATION NUMBER: 07/765212
APPLICATION DATA:
APPLICATION NUMBER: 07/790801
ATTORNEY/AGENT INFORMATION:
NAME: Hensley, Max D.
REGISTRATION NUMBER: 27,034
REFERENCE/DOCKET NUMBER: 712P4
TELECOMMUNICATION INFORMATION:
TELEPHONE: 415/266-1489
TELEFAX: 415/952-9881
TELEX: 910/371-7168
INFORMATION FOR SEQ ID NO: 27:
SEQUENCE CHARACTERISTICS:
LENGTH: 645 amino acids
TYPE: amino acid
TOPOLOGY: linear
US-08-456-201-27

Query Match 100.0%; Score 3347; DB 1; Length 645;
Best Local Similarity 100.0%; Pred. No. 1.3e-244;
Matches 645; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MSERKEGRGKGKGGKGGKPPESAAAGSQSPALPOLKEMKQESAAAGSKLVLRCTS 60
DB 1 MSERKEGRGKGKGGKGGKGGKPPESAAAGSQSPALPOLKEMKQESAAAGSKLVLRCTS 60

QY 61 SEYSSLRFFKFWKNGNELNKNPQNIKIQQKPKSELINKASLADSGEYMKVSKLGN 120
DB 61 SEYSSLRFFKFWKNGNELNKNPQNIKIQQKPKSELINKASLADSGEYMKVSKLGN 120

QY 121 DSANITIVESNEIITGMPASTEGAYVSSSPRISVSTEGANTSSSTSTTTGTSHLV 180
DB 121 DSANITIVESNEIITGMPASTEGAYVSSSPRISVSTEGANTSSSTSTTTGTSHLV 180

QY 181 KCAEKEKTCVNGGECFVKDLSNPRLKCPNEFTGDRCONVYMASFYKHLGIEFMEA 240
DB 181 KCAEKEKTCVNGGECFVKDLSNPRLKCPNEFTGDRCONVYMASFYKHLGIEFMEA 240

QY 241 EELYQKRVLTITGICALLVVGIMCVAYCKTKQKSELINKASLADSGEYMKVSKLGN 300
DB 241 EELYQKRVLTITGICALLVVGIMCVAYCKTKQKSELINKASLADSGEYMKVSKLGN 300

QY 301 PHHPNPPENVOLVNOYVSKNVISSHIVREAEATSFSTSHYTTAHHSSTTTTQPSHW 360
DB 301 PHHPNPPENVOLVNOYVSKNVISSHIVREAEATSFSTSHYTTAHHSSTTTTQPSHW 360

QY 361 SNGHTESILSESHSVIWMSSVNSRHSSPTGGPRGLNGTGPPRECNSFLRHARETDP 420
DB 361 SNGHTESILSESHSVIWMSSVNSRHSSPTGGPRGLNGTGPPRECNSFLRHARETDP 420

QY 421 RDSPHSERVVSAMTTPARMSPVDFHTPSPKPPSEMSPVSSMTVMPMAVSPFMBEE 480
DB 421 RDSPHSERVVSAMTTPARMSPVDFHTPSPKPPSEMSPVSSMTVMPMAVSPFMBEE 480

QY 481 RPLLLVTPRLREKFKDHPHQFSSPHHPNPAHDSNLSPLRIVEDEEYETTOEYEP 540
DB 481 RPLLLVTPRLREKFKDHPHQFSSPHHPNPAHDSNLSPLRIVEDEEYETTOEYEP 540

QY 541 EPVKKLANSRRAKTKPNGHIANRLEVDNSTSSQSNSESETEDEVRGDDTFFLGIQ 600
DB 541 EPVKKLANSRRAKTKPNGHIANRLEVDNSTSSQSNSESETEDEVRGDDTFFLGIQ 600

QY 601 AASLEATPAFLADSRTPNPAGRFSTQBEIQARLSSVIANQDPIAV 645
DB 601 AASLEATPAFLADSRTPNPAGRFSTQBEIQARLSSVIANQDPIAV 645


```
Db 61 SEYSSLRKFWKNGNKLNRKNKPNKI QKPKGKSELINKASLADSGEYMKVKISLGN 120
Qy 121 DSANITIVESNEIITGMPASTEGAYVSESPIRISVSTEGANTSSSTSTSTTGTSHLV 180
Db 121 DSANITIVESNEIITGMPASTEGAYVSESPIRISVSTEGANTSSSTSTSTTGTSHLV 180
Qy 181 KCAEKEKTCVNGGECFVWKDLSNPSRYLCKPCNEFTGDRCONYVNASFYKHLGIEFMEA 240
Db 181 KCAEKEKTCVNGGECFVWKDLSNPSRYLCKPCNEFTGDRCONYVNASFYKHLGIEFMEA 240
Qy 241 EELYQKRVLTITIGICIAALLVVGIMCVVAYCKTKQKQKLDHRLRQSLRSENNMMNIANG 300
Db 241 EELYQKRVLTITIGICIAALLVVGIMCVVAYCKTKQKQKLDHRLRQSLRSENNMMNIANG 300
Qy 301 PHPNPPENPVQVNVQYVSKNVISSEHIVEREAETSFSTSHYTSHTAHSTTTVTQTPSHW 360
Db 301 PHPNPPENPVQVNVQYVSKNVISSEHIVEREAETSFSTSHYTSHTAHSTTTVTQTPSHW 360
Qy 361 SNGHTESILSESHSVIWMSSVENSRRHSSPTGGPRGLNGTGPRECNFLRHARETSDSY 420
Db 361 SNGHTESILSESHSVIWMSSVENSRRHSSPTGGPRGLNGTGPRECNFLRHARETSDSY 420
Qy 421 RDSPHSERVVSAMTTPARMSPVDFTHTPSSPKSPPEMSPPVSSMTVSMPSMAVSPFMEEE 480
Db 421 RDSPHSERVVSAMTTPARMSPVDFTHTPSSPKSPPEMSPPVSSMTVSMPSMAVSPFMEEE 480
Qy 481 RPLLLVTPRLREKFDHHPQOFSFHHNPAHDSNLSPLRIVEDEYEYETTOYEYPAQ 540
Db 481 RPLLLVTPRLREKFDHHPQOFSFHHNPAHDSNLSPLRIVEDEYEYETTOYEYPAQ 540
Qy 541 EPVKLANGRRAKRTKPNGHIANRLEVDNSTSSQSSNSESETERVGEDTFFLGIQNPL 600
Db 541 EPVKLANGRRAKRTKPNGHIANRLEVDNSTSSQSSNSESETERVGEDTFFLGIQNPL 600
Qy 601 AASLEATPAFLADSRTPNAGRFSTQOEIOARLSSVIANQDPIAV 645
Db 601 AASLEATPAFLADSRTPNAGRFSTQOEIOARLSSVIANQDPIAV 645
```

RESULT 8

```
US-09-020-880-93
; Sequence 93, Application US/09020880A
; Patent No. 6136558
```

GENERAL INFORMATION:

```
; APPLICANT: Genentech, Inc.
; APPLICANT: Ballinger, Marcus D.
; APPLICANT: Jones, Jennifer T.
; APPLICANT: Fairbrother, Wayne J.
; APPLICANT: Sliwowski, Mark X.
; APPLICANT: Wells, James A.
; TITLE OF INVENTION: HERGULIN VARIANTS
; FILE REFERENCE: 14918-720CON1
; CURRENT APPLICATION NUMBER: US/09/020,880A
; EARLIER FILING DATE: 1998-02-09
; EARLIER APPLICATION NUMBER: US 60/037,581
; NUMBER OF SEQ ID NOS: 116
; SOFTWARE: FastSeq for Windows Version 3.0
; SEQ ID NO 93
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-020-880-93
```

```
Query Match 100.0%; Score 3347; DB 3; Length 645;
Best Local Similarity 100.0%; Pred. No. 1.3e-244;
Matches 645; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
```

```
Qy 1 MSERKEGRGKGKKGKRGSGKGPESAGSQSPALPQPKEMKQESAGSKLVLCRCTS 60
Db 1 MSERKEGRGKGKKGKRGSGKGPESAGSQSPALPQPKEMKQESAGSKLVLCRCTS 60
```

```
Qy 61 SEYSSLRKFWKNGNKLNRKNKPNKI QKPKGKSELINKASLADSGEYMKVKISLGN 120
Db 61 SEYSSLRKFWKNGNKLNRKNKPNKI QKPKGKSELINKASLADSGEYMKVKISLGN 120
Qy 121 DSANITIVESNEIITGMPASTEGAYVSESPIRISVSTEGANTSSSTSTSTTGTSHLV 180
Db 121 DSANITIVESNEIITGMPASTEGAYVSESPIRISVSTEGANTSSSTSTSTTGTSHLV 180
Qy 181 KCAEKEKTCVNGGECFVWKDLSNPSRYLCKPCNEFTGDRCONYVNASFYKHLGIEFMEA 240
Db 181 KCAEKEKTCVNGGECFVWKDLSNPSRYLCKPCNEFTGDRCONYVNASFYKHLGIEFMEA 240
Qy 241 EELYQKRVLTITIGICIAALLVVGIMCVVAYCKTKQKQKLDHRLRQSLRSENNMMNIANG 300
Db 241 EELYQKRVLTITIGICIAALLVVGIMCVVAYCKTKQKQKLDHRLRQSLRSENNMMNIANG 300
Qy 301 PHPNPPENPVQVNVQYVSKNVISSEHIVEREAETSFSTSHYTSHTAHSTTTVTQTPSHW 360
Db 301 PHPNPPENPVQVNVQYVSKNVISSEHIVEREAETSFSTSHYTSHTAHSTTTVTQTPSHW 360
Qy 361 SNGHTESILSESHSVIWMSSVENSRRHSSPTGGPRGLNGTGPRECNFLRHARETSDSY 420
Db 361 SNGHTESILSESHSVIWMSSVENSRRHSSPTGGPRGLNGTGPRECNFLRHARETSDSY 420
Qy 421 RDSPHSERVVSAMTTPARMSPVDFTHTPSSPKSPPEMSPPVSSMTVSMPSMAVSPFMEEE 480
Db 421 RDSPHSERVVSAMTTPARMSPVDFTHTPSSPKSPPEMSPPVSSMTVSMPSMAVSPFMEEE 480
Qy 481 RPLLLVTPRLREKFDHHPQOFSFHHNPAHDSNLSPLRIVEDEYEYETTOYEYPAQ 540
Db 481 RPLLLVTPRLREKFDHHPQOFSFHHNPAHDSNLSPLRIVEDEYEYETTOYEYPAQ 540
Qy 541 EPVKLANGRRAKRTKPNGHIANRLEVDNSTSSQSSNSESETERVGEDTFFLGIQNPL 600
Db 541 EPVKLANGRRAKRTKPNGHIANRLEVDNSTSSQSSNSESETERVGEDTFFLGIQNPL 600
Qy 601 AASLEATPAFLADSRTPNAGRFSTQOEIOARLSSVIANQDPIAV 645
Db 601 AASLEATPAFLADSRTPNAGRFSTQOEIOARLSSVIANQDPIAV 645
```

RESULT 9

```
US-09-101-544-93
; Sequence 93, Application US/09101544
; Patent No. 6387638
```

GENERAL INFORMATION:

```
; APPLICANT: Genentech, Inc.
; APPLICANT: Ballinger, Marcus D.
; APPLICANT: Jones, Jennifer T.
; APPLICANT: Fairbrother, Wayne J.
; APPLICANT: Sliwowski, Mark X.
; APPLICANT: Wells, James A.
; TITLE OF INVENTION: HERGULIN VARIANTS
; FILE REFERENCE: 14918-720CON2
; CURRENT APPLICATION NUMBER: US/09/101,544
; CURRENT FILING DATE: 1998-07-17
; PRIOR APPLICATION NUMBER: US 09/020,880
; PRIOR FILING DATE: 1998-02-09
; PRIOR APPLICATION NUMBER: US 60/037,581
; PRIOR FILING DATE: 1997-02-10
; NUMBER OF SEQ ID NOS: 116
; SOFTWARE: FastSeq for Windows Version 4.0
; SEQ ID NO 93
; LENGTH: 645
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-101-544-93
```

```
Query Match 100.0%; Score 3347; DB 3; Length 645;
Best Local Similarity 100.0%; Pred. No. 1.3e-244;
Matches 645; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
```

```
Qy 1 MSERKEGRGKGKKGKRGSGKGPESAGSQSPALPQPKEMKQESAGSKLVLCRCTS 60
```


QY 1 MSERKEGRGKGKKKGGSGKKPESAAAGSQSPALPPQKEMKQESAAAGSKLVLRCTS 60
DB 31 MSERKEGRGKGKKKGGSGKKPESAAAGSQSPALPPQKEMKQESAAAGSKLVLRCTS 90
QY 61 SYSSLRFFKFWKNGNLRNKNPQNIKIQKPKGKSELINKASLADSGEYMKCVISKLN 120
DB 91 SYSSLRFFKFWKNGNLRNKNPQNIKIQKPKGKSELINKASLADSGEYMKCVISKLN 150
QY 121 DSANANITIVESNEIITGMPASTEGAYVSSSPRISVSTEGANTSSSTSTTTGTSHLV 180
DB 151 DSANANITIVESNEIITGMPASTEGAYVSSSPRISVSTEGANTSSSTSTTTGTSHLV 210
QY 181 KCAEKEKTCVNGGECFVKDLNPSRYLCKPNEFTGDRCONVYMASFYKHLGIEFMEA 240
DB 211 KCAEKEKTCVNGGECFVKDLNPSRYLCKPNEFTGDRCONVYMASFYKHLGIEFMEA 270
QY 241 EELYQKRVLTITGICIALLVGIMCVVAYCKTKQKRLHDLRQSLRERNMMNIANG 300
DB 271 EELYQKRVLTITGICIALLVGIMCVVAYCKTKQKRLHDLRQSLRERNMMNIANG 330
QY 301 PHHPNPPPPENVOLVQYVSKNVISSSEHIVEREAETSFSTSHYTSTAHHSTTTTQTPSHW 360
DB 331 PHHPNPPPPENVOLVQYVSKNVISSSEHIVEREAETSFSTSHYTSTAHHSTTTTQTPSHW 390
QY 361 SNGHTESILSESHSVIWMSSVENSRRHSPTGGPRGLNGTGPPRECNSFLRHARETPDSY 420
DB 391 SNGHTESILSESHSVIWMSSVENSRRHSPTGGPRGLNGTGPPRECNSFLRHARETPDSY 450
QY 421 RDSPHSERVVSAMTTTPARMSPVDFHTPPSPKPPSPSEMSPPVSSMTVSMPSMAVSPMEEE 480
DB 451 RDSPHSERVVSAMTTTPARMSPVDFHTPPSPKPPSPSEMSPPVSSMTVSMPSMAVSPMEEE 510
QY 481 RPLLLVTPRLREKFDHHPQPFSSPHHPNPAHDSNLSPLASPLRIVEDEEYETTQYEPQA 540
DB 511 RPLLLVTPRLREKFDHHPQPFSSPHHPNPAHDSNLSPLASPLRIVEDEEYETTQYEPQA 570
QY 541 EPVKLANRRAKRTKPNGHIANRLEVDNNTSSQSSNSESETEDEVRGDTTFLGIONPL 600
DB 571 EPVKLANRRAKRTKPNGHIANRLEVDNNTSSQSSNSESETEDEVRGDTTFLGIONPL 630
QY 601 AASLEATPAFLADSTNPAGRFSTQEEIQARLSSVIANQDPIAV 645
DB 631 AASLEATPAFLADSTNPAGRFSTQEEIQARLSSVIANQDPIAV 675

RESULT 13

US-08-456-201-9
; Sequence 9, Application US/08456201
; Patent No. 5641869
; GENERAL INFORMATION:
; APPLICANT: Vandlen, Richard L.,
; APPLICANT: Holmes, William E.,
; TITLE OF INVENTION: Structure, Production and Use of
; TITLE OF INVENTION: Heretulin 2 Ligands
; NUMBER OF SEQUENCES: 30
; CORRESPONDENCE ADDRESSES:
; STREET: 460 Point San Bruno Blvd
; CITY: South San Francisco
; STATE: California
; COUNTRY: USA
; ZIP: 94080
; COMPUTER READABLE FORM:
; MEDIUM TYPE: 5.25 inch, 360 Kb floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: patin (Genetech)
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/456,201
; FILING DATE:
; CLASSIFICATION: 530
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: US/08/126,145

; FILING DATE:
; APPLICATION NUMBER: 07/880,917
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: 07/705256
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: 07/765212
; APPLICATION DATA:
; APPLICATION NUMBER: 07/790801
; ATTORNEY/AGENT INFORMATION:
; NAME: Hensley, Max D.
; REGISTRATION NUMBER: 27,034
; REFERENCE/DOCKET NUMBER: 712P4
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: 415/266-1489
; TELEFAX: 415/952-9881
; TELEX: 910/371-7168
; INFORMATION FOR SEQ ID NO: 9:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 732 amino acids
; TYPE: amino acid
; TOPOLOGY: linear
US-08-456-201-9
Query Match 100.0%; Score 3347; DB 1; Length 732;
Best Local Similarity 100.0%; Pred. No. 1.6e-244; Mismatches 0; Indels 0; Gaps 0;
Matches 645; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
QY 1 MSERKEGRGKGKKKGGSGKKPESAAAGSQSPALPPQKEMKQESAAAGSKLVLRCTS 60
DB 31 MSERKEGRGKGKKKGGSGKKPESAAAGSQSPALPPQKEMKQESAAAGSKLVLRCTS 90
QY 61 SEYSSLRFFKFWKNGNLRNKNPQNIKIQKPKGKSELINKASLADSGEYMKCVISKLN 120
DB 91 SEYSSLRFFKFWKNGNLRNKNPQNIKIQKPKGKSELINKASLADSGEYMKCVISKLN 150
QY 121 DSANANITIVESNEIITGMPASTEGAYVSSSPRISVSTEGANTSSSTSTTTGTSHLV 180
DB 151 DSANANITIVESNEIITGMPASTEGAYVSSSPRISVSTEGANTSSSTSTTTGTSHLV 210
QY 181 KCAEKEKTCVNGGECFVKDLNPSRYLCKPNEFTGDRCONVYMASFYKHLGIEFMEA 240
DB 211 KCAEKEKTCVNGGECFVKDLNPSRYLCKPNEFTGDRCONVYMASFYKHLGIEFMEA 270
QY 241 EELYQKRVLTITGICIALLVGIMCVVAYCKTKQKRLHDLRQSLRERNMMNIANG 300
DB 271 EELYQKRVLTITGICIALLVGIMCVVAYCKTKQKRLHDLRQSLRERNMMNIANG 330
QY 301 PHHPNPPPPENVOLVQYVSKNVISSSEHIVEREAETSFSTSHYTSTAHHSTTTTQTPSHW 360
DB 331 PHHPNPPPPENVOLVQYVSKNVISSSEHIVEREAETSFSTSHYTSTAHHSTTTTQTPSHW 390
QY 361 SNGHTESILSESHSVIWMSSVENSRRHSPTGGPRGLNGTGPPRECNSFLRHARETPDSY 420
DB 391 SNGHTESILSESHSVIWMSSVENSRRHSPTGGPRGLNGTGPPRECNSFLRHARETPDSY 450
QY 421 RDSPHSERVVSAMTTTPARMSPVDFHTPPSPKPPSPSEMSPPVSSMTVSMPSMAVSPMEEE 480
DB 451 RDSPHSERVVSAMTTTPARMSPVDFHTPPSPKPPSPSEMSPPVSSMTVSMPSMAVSPMEEE 510
QY 481 RPLLLVTPRLREKFDHHPQPFSSPHHPNPAHDSNLSPLASPLRIVEDEEYETTQYEPQA 540
DB 511 RPLLLVTPRLREKFDHHPQPFSSPHHPNPAHDSNLSPLASPLRIVEDEEYETTQYEPQA 570
QY 541 EPVKLANRRAKRTKPNGHIANRLEVDNNTSSQSSNSESETEDEVRGDTTFLGIONPL 600
DB 571 EPVKLANRRAKRTKPNGHIANRLEVDNNTSSQSSNSESETEDEVRGDTTFLGIONPL 630
QY 601 AASLEATPAFLADSTNPAGRFSTQEEIQARLSSVIANQDPIAV 645
DB 631 AASLEATPAFLADSTNPAGRFSTQEEIQARLSSVIANQDPIAV 675
RESULT 14

```

US-08-456-241-9
; Sequence 9, Application US/08456241
; Patent No. 5840525
; GENERAL INFORMATION:
; APPLICANT: Vanden, Richard L.
; APPLICANT: Holmes, William E.
; TITLE OF INVENTION: STRUCTURE, PRODUCTION AND USE OF
; TITLE OF INVENTION: HEREGULIN
; NUMBER OF SEQUENCES: 30
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Genentech, Inc.
; STREET: 460 Point San Bruno Blvd
; CITY: South San Francisco
; STATE: California
; COUNTRY: USA
; ZIP: 94080
; COMPUTER READABLE FORM:
; MEDIUM TYPE: 5.25 inch, 360 Kb floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: patin (Genentech)
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/456,241
; FILING DATE: 31-MAY-1995
; CLASSIFICATION: 435
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: 08/126145
; FILING DATE: 23-SEP-1993
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: 07/790801
; FILING DATE: 08-NOV-1991
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: 07/765212
; FILING DATE: 25-SEP-1991
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: 07/705256
; FILING DATE: 24-MAY-1991
; ATTORNEY/AGENT INFORMATION:
; NAME: Lee, Wendy M.
; REGISTRATION NUMBER: 00,000
; REFERENCE/DOCKET NUMBER: 712P4CID1
; TELEPHONE: 415/225-1994
; TELEFAX: 415/952-9881
; INFORMATION FOR SEQ ID NO: 9:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 732 amino acids
; TYPE: amino acid
; TOPOLOGY: linear
;
US-08-456-241-9
Query Match 100.0%; Score 3347; DB 2; Length 732;
Best Local Similarity 100.0%; Pred. NO. 1.6e-244;
Matches 645; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MSERKEGRGKGKKGKPSAAGSQSPALPPOLKEMKQESAAGSKLVLCRTS 60
Db 31 MSERKEGRGKGKKGKPSAAGSQSPALPPOLKEMKQESAAGSKLVLCRTS 90
QY 61 SYSSLRFRFKNGNELNKNPNQIKQKPGKSELINKASLADSGEYMKVTSKLG 120
Db 91 SYSSLRFRFKNGNELNKNPNQIKQKPGKSELINKASLADSGEYMKVTSKLG 150
QY 121 DSANITIVESNEITGMGPASTGAYVSSSEPIRISVSTEGANTSSSTSTSTGTHLV 180
Db 151 DSANITIVESNEITGMGPASTGAYVSSSEPIRISVSTEGANTSSSTSTSTGTHLV 210

181 KCAEKEKTCVNGGECFVWKDLSNPSRYLCKCPNEFTGDRCONVYMASFYKHLGIEFMEA 240
211 KCAEKEKTCVNGGECFVWKDLSNPSRYLCKCPNEFTGDRCONVYMASFYKHLGIEFMEA 270
241 EELYQKRVLTITGICIALLVGIMCVVAYCKTKQKQKHLDRQLRQSLRSENNMMNIANG 300
271 EELYQKRVLTITGICIALLVGIMCVVAYCKTKQKQKHLDRQLRQSLRSENNMMNIANG 330
301 PHHPNPPENQVQVYKQVNSSEHIVEREAETSFSTSHYTTAAHSHSTVTTQTPSHSW 360
331 PHHPNPPENQVQVYKQVNSSEHIVEREAETSFSTSHYTTAAHSHSTVTTQTPSHSW 390
361 SNGHTESILSSESHSVIWMSSVENSRRHSPTGGPGRNLNGTGPGRECSFLRHARETPOSY 420
391 SNGHTESILSSESHSVIWMSSVENSRRHSPTGGPGRNLNGTGPGRECSFLRHARETPOSY 450
421 RDSPHSERVVSAMTTPARMSPVDFTFSPSPKSPFSEMSPPVSSMTVSMPSMAVSPFMBEE 480
451 RDSPHSERVVSAMTTPARMSPVDFTFSPSPKSPFSEMSPPVSSMTVSMPSMAVSPFMBEE 510
481 RPLLLVTPPRLREKKFDHHPQFSSFHHPNPAHDSNLSLPASPLRIVEDEEYETTQYEPAQ 540
511 RPLLLVTPPRLREKKFDHHPQFSSFHHPNPAHDSNLSLPASPLRIVEDEEYETTQYEPAQ 570
541 EPVKKLANSRRAKTKPNGHIANRLEVDNSNTSSOSSNSESETEDERVGEDTFFLGIQNPL 600
571 EPVKKLANSRRAKTKPNGHIANRLEVDNSNTSSOSSNSESETEDERVGEDTFFLGIQNPL 630
601 AASLEATPAPRLADSRTPNAGRFSTQEBEIQARLSSVIANQDPIAV 645
631 AASLEATPAPRLADSRTPNAGRFSTQEBEIQARLSSVIANQDPIAV 675

RESULT 15
PCT-US92-04295A-9
; Sequence 9, Application PC/TUS9204295A
; GENERAL INFORMATION:
; APPLICANT: Genentech, Inc.
; TITLE OF INVENTION: Structure, Production and Use of
; TITLE OF INVENTION: Heregulin
; NUMBER OF SEQUENCES: 30
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Genentech, Inc.
; STREET: 460 Point San Bruno Blvd
; CITY: South San Francisco
; STATE: California
; COUNTRY: USA
; ZIP: 94080
; COMPUTER READABLE FORM:
; MEDIUM TYPE: 5.25 inch, 360 Kb floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: patin (Genentech)
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: PCT/US92/04295A
; FILING DATE: 19920521
; CLASSIFICATION:
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: 07/705256
; FILING DATE: 24-MAY-1991
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: 07/765212
; FILING DATE: 25-SEP-1991
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: 07/790801
; FILING DATE: 08-NOV-1991
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: 07/847743
; FILING DATE: 06-MAR-1992
; ATTORNEY/AGENT INFORMATION:
; NAME: Hensley, Max D.
; REGISTRATION NUMBER: 27,043

```



```
; REFERENCE/DOCKET NUMBER: 712P4
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: 415/225-1994
; TELEFAX: 415/952-9881
; TELEX: 910/371-7168
; INFORMATION FOR SEQ ID NO: 9:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 732 amino acids
; TYPE: AMINO ACID
; TOPOLOGY: linear
PCT-US92-04295A-9

Query Match      100.0%; Score 3347; DB 5; Length 732;
Best Local Similarity 100.0%; Pred. No. 1.6e-244;
Matches 645; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MSERKEGRGKGKKGKESGKPPESAGSOSPALPOLKEMKSOBSAAGSKLVLRCEYS 60
DB 1 MSERKEGRGKGKKGKESGKPPESAGSOSPALPOLKEMKSOBSAAGSKLVLRCEYS 90
QY 61 SEYSSLRFKWFKNGNELNRKNKPNQIKIQKPKSELRINKASLADSGEYMKCKVISKLG 120
DB 91 SEYSSLRFKWFKNGNELNRKNKPNQIKIQKPKSELRINKASLADSGEYMKCKVISKLG 150
QY 121 DSANATIVESNEIITGMPASTEGAYVSSSEPIRISVSTEGANTSSSTSTSTTGTSHLV 180
DB 151 DSANATIVESNEIITGMPASTEGAYVSSSEPIRISVSTEGANTSSSTSTSTTGTSHLV 210
QY 181 KCAEKEKTCVNGGECFMVKDLSNPSRYLCKNEETGDRCONYMASFYKHLGIEFMEA 240
DB 211 KCAEKEKTCVNGGECFMVKDLSNPSRYLCKNEETGDRCONYMASFYKHLGIEFMEA 270
QY 241 EELYQKRVLTITIGICALLVVGIMCVVAYCKTKQKRLHDLRQSLRSENNMMNIANG 300
DB 271 EELYQKRVLTITIGICALLVVGIMCVVAYCKTKQKRLHDLRQSLRSENNMMNIANG 330
QY 301 PPHNPNNVQVNVQVNVQVNVQVNVQVNVQVNVQVNVQVNVQVNVQVNVQVNVQVNVQVNV 360
DB 331 PPHNPNNVQVNVQVNVQVNVQVNVQVNVQVNVQVNVQVNVQVNVQVNVQVNVQVNVQV 390
QY 361 SNGHTESIILSESHSVIWMSSVNSRHSSPTGGPRGLNGTGGPRECNFLRHARETPDSY 420
DB 391 SNGHTESIILSESHSVIWMSSVNSRHSSPTGGPRGLNGTGGPRECNFLRHARETPDSY 450
QY 421 RDSPHSERVVSAMTTTPARMSPVDFHTPSGPKSPSEMSPPVSMVSMVSMVSMVSMVSMV 480
DB 451 RDSPHSERVVSAMTTTPARMSPVDFHTPSGPKSPSEMSPPVSMVSMVSMVSMVSMV 510
QY 481 RPLLLVTPRLREKFDHHPQPFSSPHNPAHDSNSLPAASPLRIVEDEYETTTQYEYPAQ 540
DB 511 RPLLLVTPRLREKFDHHPQPFSSPHNPAHDSNSLPAASPLRIVEDEYETTTQYEYPAQ 570
QY 541 EPVKKLANSERAKRTKPNGHIANRLEVDNSTSSQSSNSETEDEYVGEDTTPFLGIQNPL 600
DB 571 EPVKKLANSERAKRTKPNGHIANRLEVDNSTSSQSSNSETEDEYVGEDTTPFLGIQNPL 630
QY 601 AASLEATPAFLADSRTPNAGRFSTQEEIQARLSSVIANQDPIAV 645
DB 631 AASLEATPAFLADSRTPNAGRFSTQEEIQARLSSVIANQDPIAV 675
```

Search completed: April 12, 2005, 14:43:38
Job time : 45 secs

This Page Blank (uspto)

GenCore version 5.1.6
Copyright (c) 1993 - 2005 CompuGen Ltd.

OM protein - protein search, using sw model

Run on: April 12, 2005, 14:22:26 ; Search time 184 Seconds
(without alignments)
1795.060 Million cell updates/sec

Title: US-10-082-747A-93
Perfect score: 3347
Sequence: 1 MSERKEGRGKGKKGKRS.....QBEIQARLSSVIANQDPIAV 645

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5
Searched: 1612378 seqs, 512079187 residues
Total number of hits satisfying chosen parameters: 1612378

Minimum DB seq length: 0
Maximum DB seq length: 2000000000
Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : Uniprot_03:.*
1: uniprot_sprot:.*
2: uniprot_trembl:.*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match %	Length	ID	Description
1	3337	99.7	645	Q7RTW4	Q7rtw4 homo sapien
2	3280	98.0	637	Q7RTW3	Q7rtw3 homo sapien
3	3193.5	95.4	639	NRG1_HUMAN	Q02297 h pro-neure
4	3192.5	95.4	640	Q7RTV8	Q7rtv8 homo sapien
5	3149	94.1	645	Q6DR98	Q6dr98 mus musculu
6	3058.5	91.4	682	NRG1_RAT	P43322 r pro-neure
7	3002	89.7	782	Q9ESA5	Q9esa5 rattus norv
8	2526.5	75.5	602	NRG1_CHICK	Q05199 gallus gall
9	2395	71.6	700	Q6DR99	Q6dr99 mus musculu
10	2354.5	70.3	700	Q9ESB1	Q9esb1 rattus norv
11	2211	66.1	695	Q9ESB0	Q9esb0 rattus norv
12	2102	62.8	677	NRG1_XENLA	Q93383 xenopus lae
13	2080.5	62.2	462	Q7RTW1	Q7rtw1 homo sapien
14	1916	57.2	461	Q35947	Q35947 mesocricetu
15	1875.5	56.0	394	Q6TGK9	Q6tgk9 oryctolagus
16	1187	35.5	241	Q6PK61	Q6pk61 homo sapien
17	1183	35.3	241	Q7RTW0	Q7rtw0 homo sapien
18	1176	35.1	298	Q9ESA9	Q9esa9 rattus norv
19	1098	32.8	241	Q07112	Q07112 bos taurus
20	1071	32.0	211	Q7RTW5	Q7rtw5 homo sapien
21	1058	31.6	756	NRG2_MOUSE	P56974 mus musculu
22	1028	30.7	868	NRG2_RAT	Q35569 rattus norv
23	1003.5	30.0	317	Q9ESA3	Q9esa3 rattus norv
24	996.5	29.8	342	Q9ESAL	Q9esal rattus norv
25	993	29.7	850	NRG2_HUMAN	O14511 homo sapien
26	991	29.6	211	Q8BK18	Q8bk18 mus musculu
27	987.5	29.5	323	Q9ESA2	Q9esa2 rattus norv
28	833	24.9	167	Q8NFN2	Q8nfn2 homo sapien
29	823	24.6	422	Q7RTV9	Q7rtv9 homo sapien
30	817.5	24.4	167	Q862K0	Q862k0 bos taurus
31	503	15.0	348	Q8NFN3	Q8nfn3 homo sapien

RESULT 1

Q7RTW4	PRELIMINARY;	PRT;	645 AA.
AC	Q7RTW4;		
DT	01-MAR-2004 (Tremblrel. 26, Created)		
DT	01-MAR-2004 (Tremblrel. 26, Last sequence update)		
DT	01-MAR-2004 (Tremblrel. 26, Last annotation update)		
DE	Neuregulin 1 isoform HRG-beta1.		
GN	Name=NRG1;		
OS	Homo sapiens (Human).		
OC	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;		
OC	Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.		
OX	NCBI_TaxID=9606;		
RN	[1]_TaxID=9606;		
RP	SEQUENCE FROM N.A.		
RX	PubMed=12145742;		
RA	Steinsson H., Sigurdsson E., Steinthorsdottir V., Bjornsdottir S.,		
RA	Sigmundsson T., Ghosh S., Brynjolfsson J., Gunnarsdottir S.,		
RA	Ivarsson O., Chou T.T., Hjaltason O., Birgisdottir B., Jonsson H.,		
RA	Gudnadottir V.G., Gudmundsdottir E., Bjornsson A., Ingvarsson B.,		
RA	Ingason A., Sigfusson S., Hardardottir H., Harvey R.P., Brunner D.,		
RA	Mutel V., Gonzalo A., Lemke G., Sainz J., Johannesson G.,		
RA	Andersson T., Gudbjartsson D., Manolescu A., Frigge M.L., Gurney M.E.,		
RA	Kong A., Gulcher J.R., Petursson H., Stefansson K.;		
RL	"Neuregulin 1 and Susceptibility to Schizophrenia.";		
CC	Am. J. Hum. Genet. 71:0-0(2002).		
CC	- MISCELLANEOUS: The sequence shown here is derived from an		
DR	EMBL/GenBank/DBJ third party annotation (TPA) entry.		
DR	EMBL; BK000383; DAA00041.1; -.		
DR	HSSP; Q12780; 1HRE.		
DR	GO; GO:0005102; F:receptor binding; IEA.		
DR	GO; GO:0009790; P:embryonic development; IEA.		
DR	InterPro; IPR000742; EGF_2.		
DR	InterPro; IPR006209; EGF-like.		
DR	InterPro; IPR007110; Ig-like.		
DR	InterPro; IPR002154; Neuregulin.		
DR	Pfam; PF00008; EGF; 1.		
DR	Pfam; PF00047; ig; 1.		
DR	Pfam; PF02158; Neuregulin; 1.		
DR	PRINTS; PRO1089; NEUREGULIN.		
DR	PROSITE; PS00022; EGF 1; UNKNOWN_1.		
DR	PROSITE; PS00026; EGF 3; 1.		
DR	PROSITE; PS00835; IG Like; 1.		
SQ	SEQUENCE 645 AA; 71126 MW; 04B7AF528CDD628 CRC64;		

Query Match 99.7%; Score 3337; DB 2; Length 645;
Best Local Similarity 99.7%; Pred. No. 3.3e-175;
Matches 643; Conservative 1; Mismatches 1; Indels 0; Gaps 0;
Qy 1 MSERKEGRGKGKKGKRS.....QBEIQARLSSVIANQDPIAV 645
Db 1 MSERKEGRGKGKKGKRS.....QBEIQARLSSVIANQDPIAV 645
Qy 61 SEYSLRFRKFWKNGVNLNKNKPNQIKQPKGKSELINKASLADSGEYMKVSKLGN 120

```

Db      61 SEYSSLRFXKFKNGNELNRKNKPNQIKIQKKGKSELINKASLADSGEYMKVCKISLGN 120
QY      121 DSASANITIVESNEIITGMPASTEGAYVSSSESPIRISVSTEGANTSSSTSTSTTGTSHLV 180
Db      121 DSASANITIVESNEIITGMPASTEGAYVSSSESPIRISVSTEGANTSSSTSTSTTGTSHLV 180
QY      181 KCAEKEKTECVNGGECFMVKDLSNPSRYLCKCPNEFTGDRCONYVMAVSPYKHLGIEFMEA 240
Db      181 KCAEKEKTECVNGGECFMVKDLSNPSRYLCKCPNEFTGDRCONYVMAVSPYKHLGIEFMEA 240
QY      241 ELYQKRVLTITGICIALLVGIMCVAYCKTKQKQKLDRLQSLRSENNMNIANG 300
Db      241 ELYQKRVLTITGICIALLVGIMCVAYCKTKQKQKLDRLQSLRSENNMNIANG 300
QY      301 PHHPNPPENVOLVNOYVSKNVISSSEHIVERAEATSFSTSHYSTTAHSHSTTVTQTPSHSW 360
Db      301 PHHPNPPENVOLVNOYVSKNVISSSEHIVERAEATSFSTSHYSTTAHSHSTTVTQTPSHSW 360
QY      361 SNGHTESILSESHSVIVMSSVENSRRHSPTGPGRLNGTGGPRCNSFLRHARETPDSY 420
Db      361 SNGHTESILSESHSVIVMSSVENSRRHSPTGPGRLNGTGGPRCNSFLRHARETPDSY 420
QY      421 RDSPHSERYVSAMTTPARMSPVDFHTPPSPKSPPEMSPVSSMTVSPMAVSPFMEEE 480
Db      421 RDSPHSERYVSAMTTPARMSPVDFHTPPSPKSPPEMSPVSSMTVSPMAVSPFMEEE 480
QY      481 RPLLLVTPPRLREKFDHHPQFSSFHNNPAHDSNLSPLRIVEDEYEYETTOYEYPAQ 540
Db      481 RPLLLVTPPRLREKFDHHPQFSSFHNNPAHDSNLSPLRIVEDEYEYETTOYEYPAQ 540
QY      541 EPVKKLANSRRARKTYPNGHIANRLEVDNSTSSQSSNSESETEDEVRGVEDTFFLGIQNPL 600
Db      541 EPVKKLANSRRARKTYPNGHIANRLEVDNSTSSQSSNSESETEDEVRGVEDTFFLGIQNPL 600
QY      601 AASLEATPAFLADSRTPNAGRFSTQEEIQARLSSVIANQDPIAV 645
Db      601 AASLEATPAFLADSRTPNAGRFSTQEEIQARLSSVIANQDPIAV 645

```

RESULT 2

```

QRTW3
ID QRTW3 PRELIMINARY; PRT; 637 AA.
AC QRTW3;
DT 01-WAR-2004 (TREMELrel. 26, Created)
DT 01-WAR-2004 (TREMELrel. 26, Last sequence update)
DT 01-WAR-2004 (TREMELrel. 26, Last annotation update)
DE Neuregulin 1 isoform HRG-beta2.
GN Name=NRG1;
OS Homo sapiens (Human).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX NCBI_TaxID=9606;
RN [1]
RP SEQUENCE FROM N.A.
RX PubMed=12145742;
RA Sigurdsson H., Sigurdsson E., Steinthorsdottir V., Bjornsdottir S.,
RA Ivarsson O., Ghosh S., Brynjolfsson J., Gunnarsdottir S.,
RA Gudnadottir V.G., Gudmundsdottir E., Bjornsson A., Ingvarsson B.,
RA Ingason A., Sigfusson S., Hardardottir H., Harvey R.P., Brunner D.,
RA Mutel V., Gonzalo A., Lemke G., Sainz J., Johannesson G.,
RA Andresson T., Gudbjartsson D., Manolescu A., Frigge M.L., Gurney M.E.,
RA Kong A., Gulcher J.R., Petursson H., Stefansson K.,
RT "Neuregulin 1 and susceptibility to schizophrenia."
RL Am. J. Hum. Genet. 71:0-0(2002).
CC -1- MISCELLANEOUS: The sequence shown here is derived from an
CC EMBL/GenBank/DDBJ third party annotation (rpa) entry.
DR EMBL; BK000383; DAA0042.1; -
DR HSP; Q12780; 1HRE
DR GO; GO:0005102; F:receptor binding; IEA.
DR GO; GO:0009790; P:embryonic development; IEA.
DR InterPro; IPR000742; EGF_2.

```

```

DR InterPro; IPR006209; EGF like.
DR InterPro; IPR007110; Ig-like.
DR InterPro; IPR002154; Neuregulin.
DR Pfam; PF00008; EGF; 1.
DR Pfam; PF00047; Ig; 1.
DR Pfam; PF02158; Neuregulin; 1.
DR PRINTS; PR01089; NEUREGULIN.
DR PROSITE; PS00022; EGF_1; UNKNOWN_1.
DR PROSITE; PS00026; EGF_3; 1.
DR PROSITE; PS00835; IG_LIKE; 1.
DR SEQUENCE 637 AA; 70169 MW; 0B89DF6E2ED70333 CRC64;

Query Match      98.0%; Score 3280; DB 2; Length 637;
Best Local Similarity 98.4%; Pred. No. 4.4e-172;
Matches 635; Conservative 1; Mismatches 1; Indels 8; Gaps 1;

QY      1 MSERKEGKGKGGKKGKSGKPSAAGSQSPALPPOLKEMKQESAAAGSKLVLCRTS 60
Db      1 MSERKEGKGKGGKKGKSGKPSAAGSQSPALPPRLKEMKQESAAAGSKLVLCRTS 60
QY      61 SEYSSLRFXKFKNGNELNRKNKPNQIKIQKKGKSELINKASLADSGEYMKVCKISLGN 120
Db      61 SEYSSLRFXKFKNGNELNRKNKPNQIKIQKKGKSELINKASLADSGEYMKVCKISLGN 120
QY      121 DSASANITIVESNEIITGMPASTEGAYVSSSESPIRISVSTEGANTSSSTSTTGTSHLV 180
Db      121 DSASANITIVESNEIITGMPASTEGAYVSSSESPIRISVSTEGANTSSSTSTTGTSHLV 180
QY      181 KCAEKEKTECVNGGECFMVKDLSNPSRYLCKCPNEFTGDRCONYVMAVSPYKHLGIEFMEA 240
Db      181 KCAEKEKTECVNGGECFMVKDLSNPSRYLCKCPNEFTGDRCONYVMAVSPYKHLGIEFMEA 240
QY      241 ELYQKRVLTITGICIALLVGIMCVAYCKTKQKQKLDRLQSLRSENNMNIANG 300
Db      241 ELYQKRVLTITGICIALLVGIMCVAYCKTKQKQKLDRLQSLRSENNMNIANG 300
QY      301 PHHPNPPENVOLVNOYVSKNVISSSEHIVERAEATSFSTSHYSTTAHSHSTTVTQTPSHSW 360
Db      301 PHHPNPPENVOLVNOYVSKNVISSSEHIVERAEATSFSTSHYSTTAHSHSTTVTQTPSHSW 360
QY      361 SNGHTESILSESHSVIVMSSVENSRRHSPTGPGRLNGTGGPRCNSFLRHARETPDSY 420
Db      361 SNGHTESILSESHSVIVMSSVENSRRHSPTGPGRLNGTGGPRCNSFLRHARETPDSY 420
QY      421 RDSPHSERYVSAMTTPARMSPVDFHTPPSPKSPPEMSPVSSMTVSPMAVSPFMEEE 480
Db      421 RDSPHSERYVSAMTTPARMSPVDFHTPPSPKSPPEMSPVSSMTVSPMAVSPFMEEE 480
QY      481 RPLLLVTPPRLREKFDHHPQFSSFHNNPAHDSNLSPLRIVEDEYEYETTOYEYPAQ 540
Db      481 RPLLLVTPPRLREKFDHHPQFSSFHNNPAHDSNLSPLRIVEDEYEYETTOYEYPAQ 540
QY      541 EPVKKLANSRRARKTYPNGHIANRLEVDNSTSSQSSNSESETEDEVRGVEDTFFLGIQNPL 600
Db      541 EPVKKLANSRRARKTYPNGHIANRLEVDNSTSSQSSNSESETEDEVRGVEDTFFLGIQNPL 600
QY      601 AASLEATPAFLADSRTPNAGRFSTQEEIQARLSSVIANQDPIAV 645
Db      593 AASLEATPAFLADSRTPNAGRFSTQEEIQARLSSVIANQDPIAV 637

```

RESULT 3

```

NRG1_HUMAN
ID NRG1_HUMAN STANDARD; PRT; 639 AA.
AC Q02297; Q14667; P98202; Q02298; Q02299; Q07110; Q07111; Q12779;
AC Q12780; Q12781; Q12782; Q12783; Q12784; Q9UPE3;
DT 16-OCT-2001 (Rel. 40, Created)
DT 16-OCT-2001 (Rel. 40, Last sequence update)
DT 25-OCT-2004 (Rel. 45, Last annotation update)
DE Pre-neuregulin-1 precursor (Pro-NRG1) [contains: Neuregulin-1 (Neu
DE differentiation factor) (Herregulin) (HRG) (breast cancer cell
DE differentiation factor p45) (acetylcholine receptor inducing activity)
DE (ARIA) (Sensory and motor neuron-derived factor) (Glial growth

```

DE factor]]].

GN Name=NRGI; Synonyms=GGF, HGL, HRGA, NDF, SMDF;

OS Homo sapiens (Human).

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

CC Mammalia; Eutheria; Primates; Catarrhini; Homidae; Homo.

OX NCBI_TaxID=9606;

RN [1]

RP SEQUENCE FROM N.A. (ISOFORMS 1; 6; 7 AND 8), AND PARTIAL SEQUENCE.

RX MEDLINE=92271253; PubMed=1350381;

RA Holmes W.E., Sliwkowski M.X., Akita R.W., Henzel W.J., Lee J.,

RA Park J.W., Yansura D., Abadi N., Raab H., Lewis G.D., Shepard H.M.,

RA Kuang W.-J., Wood W.I., Goeddel D.V., Vanden R.L.; J. Biol. Chem. 268:1205-1210 (1992).

RT Identification of heregulin, a specific activator of p185erbB2.

RL Science 256:1205-1210 (1992).

RN [2]

RP SEQUENCE FROM N.A. (ISOFORMS 2; 3; 4; 6; 7 AND 8).

RX TISSUE=Kidney adenocarcinoma, and Pituitary;

RA MEDLINE=94158863; PubMed=7509448;

RA Wen D., Suggs S.V., Karunakaran D., Liu N., Cupples R.L., Luo Y.,

RA Janssen A.M., Ben-Baruch N., Trollinger D.B., Jacobsen V.L.,

RA Meng S.-Y., Lu H.S., Hu S., Chang D., Yang W., Yanigahara D.,

RA Koski R.A., Yarden Y.;

RT Structural and functional aspects of the multiplicity of Neu

RT differentiation factors.

RL Mol. Cell. Biol. 14:1909-1919 (1994).

RN [3]

RP SEQUENCE FROM N.A. (ISOFORM 1).

RX MEDLINE=92208945; PubMed=1348215; DOI=10.1016/0092-8674(92)90131-U;

RA Peles E., Bacus S.S., Koski R.A., Lu H.S., Wen D., Ogden S.G.,

RA Levy R.B., Yarden Y.;

RT Isolation of the neu/HER-2 stimulatory ligand: a 44 kd glycoprotein

RT that induces differentiation of mammary tumor cells.

RL Cell 69:205-216 (1992).

RN [4]

RP SEQUENCE FROM N.A. (ISOFORMS 8 AND 9).

RX TISSUE=Brain;

RA MEDLINE=93205115; PubMed=8096067; DOI=10.1038/362312a0;

RA Marchionni M.A., Goodearl A.D.J., Chen M.S., Birmingham-McDonogh O.,

RA Kirk C., Hendricks M., Danehy F., Misumi D., Sudhalter J.,

RA Kobayashi K., Wroblewski D., Lynch C., Baldaasare M., Hiles I.,

RA Davis J.B., Hsuan J.-J., Totty N.F., Otsu M., McBurney R.N.,

RA Waterfield M.D., Stroobant P., Gwynne D.;

RT Glial growth factors are alternatively spliced erbB2 ligands

RT expressed in the nervous system.

RL Nature 362:312-318 (1993).

RN [5]

RP SEQUENCE FROM N.A. OF GAMMA-HERGULIN FUSION PROTEIN.

RX TISSUE=Breast cancer;

RA MEDLINE=97472144; PubMed=9333014; DOI=10.1038/sj.onc.1201317;

RA Schaefer G., Fitzpatrick V.D., Sliwkowski M.X.;

RT Gamma-hergulin: a novel heregulin isoform that is an autocrine

RT growth factor for the human breast cancer cell line, MDA-MB-175.

RL Oncogene 15:1385-1394 (1997).

RN [6]

RP SEQUENCE OF 1-210 FROM N.A.

RA Schoumacher F., Herzer S., Flury N., Kueng W., Mueller H.,

RA Eppenberger U.;

RL Submitted (SEP-1997) to the EMBL/GenBank/DBJ databases.

RN [7]

RP SEQUENCE OF 19-27.

RX MEDLINE=93366731; PubMed=7689552;

RA Culouscou J.-M., Plozman G.D., Carlton G.W., Green J.M., Shoyab M.;

RT Characterization of a breast cancer cell differentiation factor that

RT specifically activates the HER4/p180erbB4 receptor.

RL J. Biol. Chem. 268:18407-18410 (1993).

RN [8]

RP CHROMOSOMAL TRANSLOCATION.

RX MEDLINE=99455251; PubMed=10523851; DOI=10.1038/sj.onc.1202950;

RA Wang X.-Z., Jolicoeur E.M., Conte N., Chaffanet M., Zhang Y.,

RA Mozziconacci M.-J., Feiner H., Birnbaum D., Febusque M.-J., Ron D.;

RT Gamma-hergulin is the product of a chromosomal translocation fusing

RT the DOC4 and HGL/NRG1 genes in the MDA-MB-175 breast cancer cell

RT line.

RL Oncogene 18:5718-5721 (1999).

RN [9]

RP CHROMOSOMAL TRANSLOCATION.

RX MEDLINE=20065180; PubMed=10597312; DOI=10.1038/sj.onc.1203136;

RA Liu X., Baker E., Eyre H.J., Sutherland G.R., Zhou M.;

RT Gamma-hergulin: a fusion gene of DOC-4 and neuregulin-1 derived from

RT a chromosome translocation.

RL Oncogene 18:7110-7114 (1999).

RN [10]

RP STRUCTURE BY NMR OF 175-241 (ISOFORM 1).

RX MEDLINE=94341264; PubMed=8062828;

RA Nagata K., Kohda D., Hatanaka H., Ichikawa S., Matsuda S.,

RA Yamamoto T., Suzuki A., Inagaki F.;

RT Solution structure of the epidermal growth factor-like domain of

RT heregulin-alpha, a ligand for p180erbB-4.

RL EMBO J. 13:3517-3523 (1994).

CC -1- FUNCTION: Direct ligand for ERBB3 and ERBB4 tyrosine kinase

CC receptors. Concomitantly recruits ERBB1 and ERBB2 coreceptors,

CC resulting in ligand-stimulated tyrosine phosphorylation and

CC activation of the ERBB receptors. The multiple isoforms perform

CC diverse functions such as inducing growth and differentiation of

CC epithelial, glial, neuronal, and skeletal muscle cells; inducing

CC expression of acetylcholine receptor in synaptic vesicles during

CC the formation of the neuromuscular junction; stimulating

CC lobuloalveolar budding and milk production in the mammary gland

CC and inducing differentiation of mammary tumor cells; stimulating

CC Schwann cell proliferation; implication in the development of the

CC myocardium such as trabeculation of the developing heart.

CC -1- SUBUNIT: The cytoplasmic domain interacts with the LIM domain

CC region of LIMK1 (by similarity).

CC -1- SUBCELLULAR LOCATION: Exists as an type I membrane protein and as

CC a proteolytically released soluble growth factor form. The

CC membrane-bound form does not seem to be active. The secreted

CC isoform 9 has a signal peptide. The isoform 8 may be nuclear.

CC -1- ALTERNATIVE PRODUCTS:

CC Event-Alternative splicing; Named isoforms=9;

CC Comment-Additional isoforms seem to exist. Isoforms have been

CC classified as type I NRGs (isoforms with an Ig domain and a

CC glycosylation domain, isoforms 1-8), type II NRGs (isoforms with

CC an Ig domain but no glycosylation domain, isoform 9) and type

CC III NRGs (isoforms with a Cys-rich domain, isoform 10). All

CC these isoforms perform distinct tissue-specific functions;

CC Name=1; Synonyms=Alpha;

CC IsoId=Q02297-1; Sequence=Displayed;

CC Name=2; Synonyms=Alpha1A;

CC IsoId=Q02297-2; Sequence=VSP_003431;

CC Name=3; Synonyms=Alpha2B;

CC IsoId=Q02297-3; Sequence=VSP_003434, VSP_003435;

CC Name=4; Synonyms=Alpha3;

CC IsoId=Q02297-4; Sequence=VSP_003432, VSP_003433;

CC Name=6; Synonyms=Betal, Beta1A;

CC IsoId=Q02297-6; Sequence=VSP_003428;

CC Name=7; Synonyms=Beta2;

CC IsoId=Q02297-7; Sequence=VSP_003427;

CC Name=8; Synonyms=Beta3, GGFHPB1;

CC IsoId=Q02297-8; Sequence=VSP_003429, VSP_003430;

CC Name=9; Synonyms=GGF2, GGFHPB2;

CC IsoId=Q02297-9; Sequence=VSP_003425, VSP_003426, VSP_003429,

CC VSP_003430;

CC Name=10; Synonyms=SMDF;

CC IsoId=Q15491-1; Sequence=External;

CC -1- TISSUE SPECIFICITY: Type I isoforms are the predominant forms

CC expressed in the endocardium. Isoform alpha is expressed in

CC breast, ovary, testis, prostate, heart, skeletal muscle, lung,

CC placenta liver, kidney, salivary gland, small intestine and brain,

CC but not in uterus, stomach, pancreas, and spleen. Isoform 3 is the

CC predominant form in mesenchymal cells and in nonneural organs,

CC whereas isoform 5 is the major neuronal form. Isoform 8 is

CC expressed in spinal cord and brain. Isoform 9 is the major form in

CC skeletal muscle cells; in the nervous system it is expressed in

CC spinal cord and brain. Also detected in adult heart, placenta,

CC lung, liver, kidney, and pancreas.

CC -1- DEVELOPMENTAL STAGE: Detectable at early embryonic ages.

Db 1 MSERKEGRGKGKGGKKGKPPESAAAGSQSPALPRLKEMKQSAAGSKVLRCETS 60
QY 61 SEYSSLRKFWKNGNLRNKNKQNIKIQQKPKGKSELINKASLADSGEYMKVSKLGN 120
Db 61 SEYSSLRKFWKNGNLRNKNKQNIKIQQKPKGKSELINKASLADSGEYMKVSKLGN 120
QY 121 DSASANTIVNESNEIITGMPASTGAGYVSSSEPIRISVSTEGANTSSSTSTSTGTSHLV 180
Db 121 DSASANTIVNESNEIITGMPASTGAGYVSSSEPIRISVSTEGANTSSSTSTSTGTSHLV 180
QY 181 KCAEKEKTFVNGGECFVWKDLSNPSRYLCKCPNEFTGDRCONYMASFYKHLGIEFMEA 240
Db 181 KCAEKEKTFVNGGECFVWKDLSNPSRYLCKCPNEFTGDRCONYMASFYKHLGIEFMEA 240
QY 241 EELYQKRVLTITGICIALLVGIMCVVAYCKTKQKPKGKSELINKASLADSGEYMKVSKLGN 300
Db 236 EELYQKRVLTITGICIALLVGIMCVVAYCKTKQKPKGKSELINKASLADSGEYMKVSKLGN 295
QY 301 PPHPNPPPPENVOLVQVSKNVISSEHIVERAEATSFSTSHYTSTAHHSTTTVTQTPSHW 360
Db 296 PPHPNPPPPENVOLVQVSKNVISSEHIVERAEATSFSTSHYTSTAHHSTTTVTQTPSHW 355
QY 361 SNGHTESIISSESHSVIMSSVENSRHSSPTGGPRGLNGTGPPRECNSFLRHARETPDSY 420
Db 356 SNGHTESIISSESHSVIMSSVENSRHSSPTGGPRGLNGTGPPRECNSFLRHARETPDSY 415
QY 421 RDSPHSERVYSAMTTTPARMSPVDFHTPPSPKPPSEMSPPVSSMTVMPMSVAPPMEE 480
Db 416 RDSPHSERVYSAMTTTPARMSPVDFHTPPSPKPPSEMSPPVSSMTVMPMSVAPPMEE 475
QY 481 RPLLLVTPRLREKFKDHPHQFSSPHHNPADNSLSPASPLRIVEDEEYETTQYEYPAQ 540
Db 476 RPLLLVTPRLREKFKDHPHQFSSPHHNPADNSLSPASPLRIVEDEEYETTQYEYPAQ 535
QY 541 EPVKKLANSRRARAKTKPNGHIANRLEVDNTSSQSSNSESETEDEVRGDDTTPFLGIONPL 600
Db 536 EPVKKLANSRRARAKTKPNGHIANRLEVDNTSSQSSNSESETEDEVRGDDTTPFLGIONPL 595
QY 601 AASLEATPAFLADSRTPAGRFSTQEEIQARLSSVIANQDPIAV 645
Db 596 AASLEATPAFLADSRTPAGRFSTQEEIQARLSSVIANQDPIAV 640

RESULT 5

Q6DR98
ID Q6DR98 PRELIMINARY; PRT; 645 AA.
AC Q6DR98;
DT 25-OCT-2004 (TrEMBLrel. 28, Created)
DT 25-OCT-2004 (TrEMBLrel. 28, Last sequence update)
DT 25-OCT-2004 (TrEMBLrel. 28, Last annotation update)
DE Neuregulin-1 type I betal-a.
GN Name=Nrgl;
OS Mus musculus (Mouse).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX NCBI_TaxID=10090;
RN [1]
RP SEQUENCE FROM N.A.
RC STRAIN=C57Bl6J;
RA Anton E.S., Ghassghaei H.T., Weber J.L., McCann C., Fischer T.M.,
RA Cheung I.D., Gassmann M., Messing A., Klein R., Schwab M.H.,
RA Lloyd K.C., Lai C.;
RL Submitted (JUN-2004) to the EMBL/GenBank/DBJ databases.
CC -1- SIMILARITY: Contains 1 EGF-like domain.
DR EMBL; AY648976; AAT68241.1; -
DR GO; GO:0005102; F:receptor binding; IEA.
DR GO; GO:0009790; P:embryonic development; IEA.
DR InterPro; IPR000742; EGF 2.
DR InterPro; IPR006209; EGF-like.
DR InterPro; IPR006210; EGF.
DR InterPro; IPR003599; Ig.
DR InterPro; IPR007110; Ig-like.
DR InterPro; IPR003598; Ig_c2.

DR InterPro; IPR002154; Neuregulin.
DR Pfam; PF00008; EGF; 1.
DR Pfam; PF00047; ig; 1.
DR Pfam; PF02158; Neuregulin; 1.
DR PRINTS; PR01089; NEUREGULIN.
DR SMART; SM00181; EGF; 1.
DR SMART; SM00409; ig; 1.
DR SMART; SM00408; IGC2; 1.
DR PROSITE; PS00022; EGF 1; UNKNOWN_1.
DR PROSITE; PS00026; EGF 3; 1.
DR PROSITE; PS00835; IG_LIKE; 1.
KW EGF-like domain.
SQ SEQUENCE 645 AA; 71381 MW; 75755AEF73F55047 CRC64;
Query Match 94.1%; Score 3149; DB 2; Length 645;
Best Local Similarity 93.0%; Pred. No. 6.9e-165;
Matches 600; Conservative 21; Mismatches 24; Indels 0; Gaps 0;
QY 1 MSERKEGRGKGKGGKKGKPPESAAAGSQSPALPRLKEMKQSAAGSKVLRCETS 60
Db 1 MSERKEGRGKGKGGKKGKPPESAAAGSQSPALPRLKEMKQSAAGSKVLRCETS 60
QY 61 SEYSSLRKFWKNGNLRNKNKQNIKIQQKPKGKSELINKASLADSGEYMKVSKLGN 120
Db 61 SEYSSLRKFWKNGNLRNKNKQNIKIQQKPKGKSELINKASLADSGEYMKVSKLGN 120
QY 121 DSASANTIVNESNEIITGMPASTGAGYVSSSEPIRISVSTEGANTSSSTSTSTGTSHLV 180
Db 121 DSASANTIVNESNEIITGMPASTGAGYVSSSEPIRISVSTEGANTSSSTSTSTGTSHLV 180
QY 181 KCAEKEKTFVNGGECFVWKDLSNPSRYLCKCPNEFTGDRCONYMASFYKHLGIEFMEA 240
Db 181 KCAEKEKTFVNGGECFVWKDLSNPSRYLCKCPNEFTGDRCONYMASFYKHLGIEFMEA 240
QY 241 EELYQKRVLTITGICIALLVGIMCVVAYCKTKQKPKGKSELINKASLADSGEYMKVSKLGN 300
Db 241 EELYQKRVLTITGICIALLVGIMCVVAYCKTKQKPKGKSELINKASLADSGEYMKVSKLGN 300
QY 301 PPHPNPPPPENVOLVQVSKNVISSEHIVERAEATSFSTSHYTSTAHHSTTTVTQTPSHW 360
Db 301 PPHPNPPPPENVOLVQVSKNVISSEHIVERAEATSFSTSHYTSTAHHSTTTVTQTPSHW 360
QY 361 SNGHTESIISSESHSVIMSSVENSRHSSPTGGPRGLNGTGPPRECNSFLRHARETPDSY 420
Db 361 SNGHTESIISSESHSVIMSSVENSRHSSPTGGPRGLNGTGPPRECNSFLRHARETPDSY 420
QY 421 RDSPHSERVYSAMTTTPARMSPVDFHTPPSPKPPSEMSPPVSSMTVMPMSVAPPMEE 480
Db 421 RDSPHSERVYSAMTTTPARMSPVDFHTPPSPKPPSEMSPPVSSMTVMPMSVAPPMEE 480
QY 481 RPLLLVTPRLREKFKDHPHQFSSPHHNPADNSLSPASPLRIVEDEEYETTQYEYPAQ 540
Db 481 RPLLLVTPRLREKFKDHPHQFSSPHHNPADNSLSPASPLRIVEDEEYETTQYEYPAQ 540
QY 541 EPVKKLANSRRARAKTKPNGHIANRLEVDNTSSQSSNSESETEDEVRGDDTTPFLGIONPL 600
Db 541 EPVKKLANSRRARAKTKPNGHIANRLEVDNTSSQSSNSESETEDEVRGDDTTPFLGIONPL 600
QY 601 AASLEATPAFLADSRTPAGRFSTQEEIQARLSSVIANQDPIAV 645
Db 601 AASLEATPAFLADSRTPAGRFSTQEEIQARLSSVIANQDPIAV 645

RESULT 6

NRG1 RAT
ID NRG1 RAT STANDARD; PRT; 662 AA.
AC P43323; P43324; P43325; P43326; P43327; P43328;
DT 16-OCT-2001 (Rel. 40, Created)
DT 16-OCT-2001 (Rel. 40, Last sequence update)
DT 05-JUL-2004 (Rel. 44, Last annotation update)
DE Pro-neuregulin-1 precursor (Pro-NRG1) [Contains: Neuregulin-1 (Neu differentiation factor) (Heregulin) (HRG) (Acetylcholine receptor inducing activity) (ARIA) (Sensory and motor neuron-derived factor)]

DE (Glial growth factor)]].
GN Name=Nrg1; Synonyms=Ndf;
OS Rattus norvegicus (Rat).
OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
OX NCBI_TaxId=10116;
RN [1]
RP SEQUENCE FROM N.A., AND ALTERNATIVE SPLICING.
RX TISSUE=Fibroblast;
RA MEDLINE=94158863; PubMed=7509448;
RA Wen D., Sugis S.V., Karunakaran D., Liu N., Cupples R.L., Luo Y.,
RA Jansen A.M., Ben-Baruch N., Trollinger D.B., Jacobsen V.L.,
RA Meng S.-Y., Lu H.S., Hu S., Chang D., Yang W., Yanigahara D.,
RA Koski R.A., Yarden Y.;
RT "Structural and functional aspects of the multiplicity of Neu
RT differentiation factors";
RT Mol. Cell. Biol. 14:1909-1919(1994).
RN [2]
RP SEQUENCE FROM N.A. (ISOFORM ALPHA2C/NDFA4), AND PARTIAL SEQUENCE.
RX TISSUE=Fibroblast;
RA MEDLINE=92208945; PubMed=1349853; DOI=10.1016/0092-8674(92)90456-M;
RA Wen D., Sugis S.V., Cupples R., Sugis S.V., Bacus S.S., Luo Y.,
RA Trall G., Hu S., Silbiger S.M., Levy R.B., Koski R.A., Lu H.S.,
RA Yarden Y.;
RT "Neu differentiation factor: a transmembrane glycoprotein containing
RT an EGF domain and an immunoglobulin homology unit";
RT Cell 69:559-572(1992).
RN [3]
RP SEQUENCE OF 14-36.
RX MEDLINE=92208945; PubMed=1349853; DOI=10.1016/0092-8674(92)90456-M;
RA Peles E., Bacus S.S., Koski R.A., Lu H.S., Wen D., Ogden S.G.,
RA Levy R.B., Yarden Y.;
RT "Isolation of the neu/HER-2 stimulatory ligand: a 44 kd glycoprotein
RT that induces differentiation of mammary tumor cells";
RT Cell 69:205-216(1992).
RN [4]
RP REGULATION OF PROCESSING (ISOFORM ALPHA2C/NDFA4).
RX MEDLINE=99069430; PubMed=9852099; DOI=10.1074/jbc.273.51.34335;
RA Liu X., Hwang H., Cao L., Wen D., Liu N., Graham R.M., Zhou M.;
RT "Release of the neu/HER-2 stimulatory ligand requires its
RT cytoplasmic tail";
RT J. Biol. Chem. 273:20525-20534(1998).
RN [5]
RP INTERACTION WITH LIMK1.
RX MEDLINE=98352096; PubMed=9685409; DOI=10.1074/jbc.273.32.20525;
RA Wang J.Y., Frenzel K.E., Wen D., Falls D.L.;
RT "Transmembrane neu/HER-2 interact with LIM kinase 1, a cytoplasmic
RT protein kinase implicated in development of visuospatial cognition";
RL J. Biol. Chem. 273:20525-20534(1998).
CC -!- FUNCTION: Direct ligand for ERBB3 and ERBB4 tyrosine kinase
CC receptors. Concomitantly recruits ERBB1 and ERBB2 coreceptors,
CC resulting in ligand-stimulated tyrosine phosphorylation and
CC activation of the ERBB receptors. The multiple isoforms perform
CC diverse functions such as inducing growth and differentiation of
CC epithelial, glial, neuronal, and skeletal muscle cells; inducing
CC expression of acetylcholine receptor in synaptic vesicles during
CC the formation of the neuromuscular junction; stimulating
CC lobuloalveolar budding and milk production in the mammary gland
CC and inducing differentiation of mammary tumor cells; stimulating
CC Schwann cell proliferation; implication in the development of the
CC myocardium such as trabeculation of the developing heart (By
CC similarity).
CC -!- SUBUNIT: The cytoplasmic domain interacts with the LIM domain
CC region of LIMK1.
CC -!- SUBCELLULAR LOCATION: Exists as a type I membrane protein and as a
CC proteolytically released soluble growth factor form. The membrane-
CC bound form does not seem to be active.
CC -!- ALTERNATIVE PRODUCTS:
CC Event-Alternative splicing: Named isoforms=8;
CC Comment=Additional isoforms seem to exist;
CC Name=Beta4; Synonyms=NDFA2A;
CC IsoId=P43322-1; Sequence=Displayed;
CC Name=Alpha2A; Synonyms=NDFA38;

CC IsoId=P43322-2; Sequence=VSP_003436;
CC Name=Alpha2B; Synonyms=NDFA19;
CC IsoId=P43322-3; Sequence=VSP_003436, VSP_003443, VSP_003444;
CC Name=Alpha2C; Synonyms=NDFA4;
CC IsoId=P43322-4; Sequence=VSP_003436, VSP_003442;
CC Name=Beta1;
CC IsoId=P43322-5; Sequence=VSP_003437;
CC Name=Beta2; Synonyms=NDFA0;
CC IsoId=P43322-6; Sequence=VSP_003440, VSP_003441;
CC Name=Beta2A; Synonyms=NDFA22;
CC IsoId=P43322-7; Sequence=VSP_003440;
CC Name=Beta3; Synonyms=NDFA4;
CC IsoId=P43322-8; Sequence=VSP_003438, VSP_003439;
CC -!- TISSUE SPECIFICITY: Widely expressed. Most tissues contain alpha2A
CC and alpha2B isoforms. Alpha2 and beta2 are the predominant forms
CC in mesenchymal and nonneural organs. Beta1 is enriched in brain
CC and spinal cord, but not in muscle and heart. Alpha2C is highly
CC expressed in spinal cord, moderately in lung, brain, ovary, and
CC stomach, in low amounts in the kidney, skin and heart and not
CC detected in the liver, spleen, and placenta.
CC -!- DOMAIN: The cytoplasmic domain may be involved in the regulation of
CC trafficking and proteolytic processing. Regulation of the
CC proteolytic processing involves initial intracellular domain
CC dimerization.
CC -!- DOMAIN: ERBB receptor binding is elicited entirely by the EGF-like
CC domain.
CC -!- PTM: Proteolytic cleavage close to the plasma membrane on the
CC external face leads to the release of the soluble growth factor
CC form.
CC -!- PTM: Extensive glycosylation precedes the proteolytic cleavage.
CC -!- SIMILARITY: Belongs to the neu/HER-2 family.
CC -!- SIMILARITY: Contains 1 EGF-like domain.
CC -!- SIMILARITY: Contains 1 immunoglobulin-like C2-type domain.
CC -----
CC This SWISS-PROT entry is copyright. It is produced through a collaboration
CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC the European Bioinformatics Institute. There are no restrictions on its
CC use by non-profit institutions as long as its content is in no way
CC modified and this statement is not removed. Usage by and for commercial
CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>
CC or send an email to license@isb-sib.ch).
CC -----
CC EMBL; U02315; AAA19940.1; -
CC EMBL; U02316; AAA19941.1; -
CC EMBL; U02317; AAA19942.1; -
CC EMBL; U02318; AAA19943.1; -
CC EMBL; U02319; AAA19944.1; -
CC EMBL; U02320; AAA19945.1; -
CC EMBL; U02321; AAA19946.1; -
CC EMBL; U02322; AAA19947.1; -
CC EMBL; U02323; AAA19948.1; -
CC EMBL; U02324; AAA19949.1; -
CC EMBL; M92430; -; NOT ANNOTATED_CDS.
CC PIR; I61718; I61718.
CC PIR; I61719; I61719.
CC PIR; I61722; I61722.
CC HSSP; Q12780; 1HRE.
CC RGD; 621341; Nrg1.
CC InterPro; IPR000742; EGF_2.
CC InterPro; IPR006209; EGF_like.
CC InterPro; IPR006210; IEGF.
CC InterPro; IPR007110; IG-like.
CC InterPro; IPR003598; IG_c2.
CC InterPro; IPR002154; Neuregulin.
CC Pfam; PF00008; EGF; 1.
CC Pfam; PF00047; Ig; 1.
CC Pfam; PF02158; Neuregulin; 1.
CC PRINTS; PR01089; NEUREGULIN.
CC SMART; SM00181; EGF; 1.
CC SMART; SM00408; IGC2; 1.
CC PROSITE; PS00022; EGF_1; 1.
CC PROSITE; PS01186; EGF_2; FALSE_NEG.
CC PROSITE; PS50026; EGF_3; 1.

QY 288 RSRNNMNIANGPHHPNPPENVOLVNOYVSKNVISSHHIVERAEATSFSTSHYTSTA 347
DB 343 RSRNNMNIANGPHHPNPPENVOLVNOYVSKNVISSHHIVERAEATSFSTSHYTSTA 402
QY 348 HSTTVTQTPSHWSNGHTESILSESHSVTMSVSSVNSHRHSPGPRGLNGTGPRCN 407
DB 403 HSTTVTQTPSHWSNGHTESILSESHSVTMSVSSVNSHRHSPGPRGLNGTGPRCN 462
QY 408 SFLRHARETPDSYRSPHSRYSVAMTTPARMSPVDFHTPPSPKPPSEMPPVSSMTVS 467
DB 463 SFLRHARETPDSYRSPHSRYSVAMTTPARMSPVDFHTPPSPKPPSEMPPVSSMTVS 522
QY 468 MFSMAVSPMEERPLLVTPLRLREKPDHHPQFSSFHHPNPAHDSNLSPLRIVED 527
DB 523 MFSVAVSPVEERPLLVTPLRLREKPDHHPQFSSFHHPNPAHDSNLSPLRIVED 582
QY 528 EYVETTOEYEPQEPVKLANRRRAKRTKPNGHIANRLVDNTSSQSSNSESETERV 587
DB 583 EYVETTOEYEPQEPVKLANRRRAKRTKPNGHIANRLVDNTSSQSSNSESETERV 642
QY 588 GEDTFLGIONPLAASLEATPAFLADSTNPAFLADSTNPAFLADSTNPAFLADSTNPA 645
DB 643 GEDTFLGIONPLAASLEATPAFLADSTNPAFLADSTNPAFLADSTNPAFLADSTNPA 700

RESULT 10
Q9ESB1 PRELIMINARY; PRT; 700 AA.
AC Q9ESB1; (TrEMBLrel. 16, Created)
DT 01-MAR-2001 (TrEMBLrel. 16, Last sequence update)
DT 01-MAR-2004 (TrEMBLrel. 26, Last annotation update)
DE SMDF neuregulin beta la.
GN Name=Nrg1;
OS Rattus norvegicus (Rat).
OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
OX NCBI_TaxID=10116;
RN [1]
RP SEQUENCE FROM N.A.
RC STRAIN=Sprague-Dawley;
RA Carroll S.L., Anderson K.D., Frohnert P.W.;
RL Submitted (OCT-1999) to the EMBL/GenBank/DBJ databases.
CC -!- SIMILARITY: Contains 1 EGF-like domain.
DR EMBL; AF194438; AAG2827.1; -.
DR HSSP; Q12780; 1HRE.
DR GO; GO:0005102; F:receptor binding; IEA.
DR GO; GO:0009790; P:embryonic development; IEA.
DR InterPro; IPR000742; EGF 2.
DR InterPro; IPR006209; EGF-like.
DR InterPro; IPR002114; HPr_Serp_S.
DR InterPro; IPR006210; IEGF.
DR Pfam; PF02158; Neuregulin; 1.
DR PRINTS; PR01089; NEUREGULIN.
DR SMART; SM00181; EGF; 1.
DR PROSITE; PS00022; EGF_1; UNKNOWN_1.
DR PROSITE; PS00026; EGF_3; 1.
DR PROSITE; PS00589; PTS_HPR_SER; UNKNOWN_1.
KW EGF-like domain.
SQ SEQUENCE 700 AA; 76386 MW; 2F8111B17ECC49DA CRC64;

Query Match 70.38; Score 2354.5; DB 2; Length 700;
Best Local Similarity 80.68; Pred. No. 3.3e-121;
Matches 456; Conservative 29; Mismatches 52; Indels 29; Gaps 4;

QY 107 SGEYMKVSKLGNDSASANITVESNEIITGMPA-----STEGAYVSS 150
DB 137 SSEAYTSPVSK-AQSEAGAHVTQGDHAAVASEPSAVPTRKNRLSAFPHPHSTAPPPSP 195
QY 151 ESPRISVSTEGANTSS-----STSTSTTGTSHLVKCAEKEKTCVNGGECFTV 199

DB 196 ARTPEVTPKSGTQPQTETNLQTA PKLSTSTSTTGTSHLVKCAEKEKTCVNGGECFTV 255
QY 200 KDLSPSRYLCKPNFTGDRCONYVMAFYKHLGIEFMEAEELYOKRVLTITGICALL 259
DB 256 KDLSPSRYLCKPNFTGDRCONYVMAFYKHLGIEFMEAEELYOKRVLTITGICALL 315
QY 260 VVGIMCVAVCKTKKORLHDLRSLRSERNMNIANGPHHPNPPENVOLVNOYVVS 319
DB 316 VVGIMCVAVCKTKKORLHDLRSLRSERNMNIANGPHHPNPPENVOLVNOYVVS 375
QY 320 KNVISSEHIVERAEATSFSTSHYTSTAHSHTTQTTPSHWSNGHTESILSESHSVTMS 379
DB 376 KNVISSEHIVERAEATSFSTSHYTSTAHSHTTQTTPSHWSNGHTESILSESHSVTMS 435
QY 380 SVENSRHSSSTGPRGLNGTGPRCNLSFLRHARETPDSYRSPHSRYSVAMTTPARM 439
DB 436 SVENSRHSSSTGPRGLNGTGPRCNLSFLRHARETPDSYRSPHSRYSVAMTTPARM 494
QY 440 SPVDFHTPPSPKPPSEMSPVSMVSPMEERPLLVTPLRLREKPFDDH 499
DB 495 SPVDFHTPPSPKPPSEMSPVSMVSPMEERPLLVTPLRLREKPFDDH 554
QY 500 PQQSSSFHHPNPAHDSNLSPLRIVEDEYETTOEYEPQEPVKLANRRRAKRTKPN 559
DB 555 PQQSSSFHHPNPAHDSNLSPLRIVEDEYETTOEYEPQEPVKLANRRRAKRTKPN 614
QY 560 HIANRLVDNTSSQSSNSESETERVGDTPFLGIONPLAASLEATPAFLADSTNPA 619
DB 615 HIANRLVDNTSSQSSNSESETERVGDTPFLGIONPLAASLEATPAFLADSTNPA 674
QY 620 AGFSTQEEIQARLSSVIANQDPIAV 645
DB 675 AGFSTQEEIQARLSSVIANQDPIAV 700

RESULT 11
Q9ESB0 PRELIMINARY; PRT; 695 AA.
AC Q9ESB0; (TrEMBLrel. 16, Created)
DT 01-MAR-2001 (TrEMBLrel. 16, Last sequence update)
DT 01-MAR-2004 (TrEMBLrel. 26, Last annotation update)
DE SMDF neuregulin alpha 2a.
GN Name=Nrg1;
OS Rattus norvegicus (Rat).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
OX NCBI_TaxID=10116;
RN [1]
RP SEQUENCE FROM N.A.
RC STRAIN=BDIX;
RA Carroll S.L., Anderson K.D., Frohnert P.W.;
RL Submitted (OCT-1999) to the EMBL/GenBank/DBJ databases.
CC -!- SIMILARITY: Contains 1 EGF-like domain.
DR EMBL; AF194439; AAG28428.1; -.
DR HSSP; Q12780; 1HRE.
DR GO; GO:0005102; F:receptor binding; IEA.
DR GO; GO:0009790; P:embryonic development; IEA.
DR InterPro; IPR000742; EGF 2.
DR InterPro; IPR006209; EGF-like.
DR InterPro; IPR002114; HPr_Serp_S.
DR InterPro; IPR006210; IEGF.
DR InterPro; IPR002154; Neuregulin.
DR Pfam; PF02158; Neuregulin; 1.
DR PRINTS; PR01089; NEUREGULIN.
DR SMART; SM00181; EGF; 1.
DR PROSITE; PS00022; EGF_1; 1.
DR PROSITE; PS01186; EGF_2; 1.
DR PROSITE; PS00026; EGF_3; 1.
DR PROSITE; PS00589; PTS_HPR_SER; UNKNOWN_1.
KW EGF-like domain.
SQ SEQUENCE 695 AA; 75646 MW; 5277F2CBA2FB6878 CRC64;

Query Match 66.1%; Score 2211; DB 2; Length 695;
 Best Local Similarity 77.6%; Pred. No. 2.5e-113;
 Matches 440; Conservative 33; Mismatches 58; Indels 36; Gaps 8;

QY 107 SGEYCKVYKLGNDASANIITIVESNEITGPAS--TEGAYVSS-----ESP 153
 DB 137 SSEAYTSPVSK-AQSEAGAHVTVOGDHAAVASEPSAVPTRKNRLSPFPFHPHTAPPFSP 195
 QY 154 IRI-SYSTEGANTSS-----STSTSTTGTSHLVKCAEKEKTCVNGGSCPMV 199
 DB 196 ARTPEVTPKSGTOPOTETNLTQAPKLSTSTSTTGTSHLVKCAEKEKTCVNGGSCFTV 255
 QY 200 KDLNPNRYLYCKPCNFTGDRQNYWASPYKHLGIEPME-ABELYQKRVLTITGICIAL 258
 DB 256 KDLNPNRYLYCKPCNFTGDRQNYWASPYKHLGIEPME-ABELYQKRVLTITGICIAL 309
 QY 259 LVVGIMCVAYCKTKQKQLHDLRLQSLRSERNMMNANGPHHNPENNVQV 318
 DB 310 LVVGIMCVAYCKTKQKQLHDLRLQSLRSERNMMNANGPHHNPENNVQV 369
 QY 319 SKNVISEHIVERAEATSTSTSHYTTTAHSTTTVTPSHSNGHTEGILSHSHVIM 378
 DB 370 SKNVISEHIVERAEATSTSTSHYTTTAHSTTTVTPSHSNGHTEGILSHSHVIM 429
 QY 379 SSVENSRHSPTGCGRLNGTGGPCRCNSFLRHARETSDSYRSDSPHSRYVSAMTTPAR 438
 DB 430 SSVENSRHSPTGCGRLNGTGGPCRCNSFLRHARETSDSYRSDSPHSRYVSAMTTPAR 488
 QY 439 MSPVDHPTSSPKSPSEMSPPVSSMTVSPMSVAVSPFVEEERPLLVTTPRLREKFPD 498
 DB 489 MSPVDHPTSSPKSPSEMSPPVSSMTVSPMSVAVSPFVEEERPLLVTTPRLREKFPD 548
 QY 499 HPQOFSFHNPAHDSNLPASPLRIVEDEEYETTOYEPAPQSPVKKLANSRRAKTKEN 558
 DB 549 HPQOFSFHNPAHDSNLPASPLRIVEDEEYETTOYEPAPQSPVKKLANSRRAKTKEN 608
 QY 559 GHIANRLEVDNSTSSQSSSESETEDEYVGEDTPFLGIGNQNLAAASLEATPAFLADSRN 618
 DB 609 GHIANRLEVDNSTSSQSSSESETEDEYVGEDTPFLGIGNQNLAAASLEATPAFLADSRN 668
 QY 619 PAGRFSTQBEIQARLSSVTANQDPIAV 645
 DB 669 PAGRFSTQBEIQARLSSVTANQDPIAV 695

RESULT 12

NRG1_XENLA STANDARD; PRT; 677 AA.
 AC O93383; Q9W6N0;
 DT 16-OCT-2001 (Rel. 40, Created)
 DT 16-OCT-2001 (Rel. 40, Last sequence update)
 DT 05-JUL-2004 (Rel. 44, Last annotation update)
 DE Pro-neuregulin-1 precursor (Pro-NRG1) [Contains: Neuregulin-1].
 GN Names=NRG1;
 OS Xenopus laevis (African clawed frog).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Amphibia; Batrachia; Anura; Mesobatrachia; Pipidae; Pipidae;
 OC Xenopodinae; Xenopus.
 OC NCBI_TaxID=8355;
 RN [1]
 RP SEQUENCE FROM N.A. (ISOFORM ALPHA), AND ALTERNATIVE SPLICING.
 RX MEDLINE=98352126; PubMed=9685585; DOI=10.1016/S0169-328X(98)00085-0;
 RA Yang J.F., Zhou H., Pun S., Ip N.Y., Peng H.B., Tsai K.W.K.;
 RT "Cloning of cDNAs encoding xenopus neuregulin: expression in myotomal
 muscle during embryo development."
 RL Brain Res. Mol. Brain Res. 58:59-73(1998).
 RN [2]
 RP SEQUENCE FROM N.A. (ISOFORM CRD).
 RX MEDLINE=99316087; PubMed=10383827; DOI=10.1006/mcne.1999.0759;
 RA Yang J.F., Zhou H., Choi R.C., Ip N.Y., Peng H.B., Tsai K.W.K.;
 RT "A cysteine-rich form of Xenopus neuregulin induces the expression of
 acetylcholine receptors in cultured myotubes.";

RL Mol. Cell. Neurosci. 13:415-429(1999).
 CC -!- FUNCTION: Direct ligand for the ERBB tyrosine kinase receptors.
 CC Induces expression of acetylcholine receptor in synaptic nuclei.
 CC -!- SUBCELLULAR LOCATION: Exists as a type I membrane protein and as a
 CC proteolytically released soluble growth factor form. The membrane-
 CC bound form does not seem to be active (By similarity).
 CC -!- ALTERNATIVE PRODUCTS:
 CC Event=Alternative splicing; Named isoforms=2;
 CC Comment=Additional isoforms seem to exist. Isoforms have alpha-
 CC or beta-type EGF-like domains;
 CC Name=Alpha;
 CC IsoId=O93383-1; Sequence=Displayed;
 CC Name=CRD; Synonyms=CRD-NRG1, Cysteine-rich domain;
 CC IsoId=O93383-2; Sequence=VSP 003449, VSP 003450;
 CC -!- TISSUE SPECIFICITY: Isoform alpha is expressed in brain and
 CC muscle. Isoform CRD is expressed in brain and spinal cord, but at
 CC very low level in muscle.
 CC -!- DEVELOPMENTAL STAGE: Strong expression in developing brain and
 CC spinal cord of the embryo. Also expressed in the myotomal muscle.
 CC -!- DOMAIN: The cytoplasmic domain may be involved in the regulation
 CC of trafficking and proteolytic processing. Regulation of the
 CC proteolytic processing involves initial intracellular domain
 CC dimerization (By similarity).
 CC -!- DOMAIN: ERBB receptor binding is elicited entirely by the EGF-like
 CC domain.
 CC -!- PTM: Proteolytic cleavage close to the plasma membrane on the
 CC external face leads to the release of the soluble growth factor
 CC form.
 CC -!- PTM: Extensive glycosylation precedes the proteolytic cleavage (By
 CC similarity).
 CC -!- SIMILARITY: Belongs to the neuregulin family.
 CC -!- SIMILARITY: Contains 1 EGF-like domain.
 CC -!- SIMILARITY: Contains 1 immunoglobulin-like C2-type domain.
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration
 CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
 CC the European Bioinformatics Institute. There are no restrictions on its
 CC use by non-profit institutions as long as its content is in no way
 CC modified and this statement is not removed. Usage by and for commercial
 CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>
 CC or send an email to license@isb-sib.ch).
 CC -----
 CC EMBL; AF076618; AAC36804.1; -;
 CC EMBL; AF142632; AAD33893.1; -;
 CC HSP; O12780; 1HRE.
 CC InterPro; IPR000742; EGF 2.
 CC InterPro; IPR006209; EGF-like.
 CC InterPro; IPR007110; Ig-like.
 CC InterPro; IPR002154; Neuregulin.
 CC Pfam; PF00008; EGF; 1.
 CC Pfam; PF00047; ig; 1.
 CC Pfam; PF02158; Neuregulin; 1.
 CC PRINTS; PRO1089; NEUREGULIN.
 CC PROSITE; PS00022; EGF 1; 1.
 CC PROSITE; PS01186; EGF 2; 1.
 CC PROSITE; PS00026; EGF 3; 1.
 CC PROSITE; PS00835; IG Like; 1.
 CC Alternative splicing; EGF-like domain; Glycoprotein; Growth factor;
 CC Immunoglobulin domain; Transmembrane.
 CC Neuregulin-1 (By similarity).
 CC Pro-neuregulin-1, membrane-bound form (By
 CC similarity).
 CC CHAIN 1 677
 CC DOMAIN 1 260
 CC TRANSMEM 261 280
 CC DOMAIN 281 677
 CC DOMAIN 37 132
 CC DOMAIN 188 232
 CC DISULFID 57 116
 CC DISULFID 192 206
 CC DISULFID 200 220
 CC DISULFID 222 231
 CC DOMAIN 1 25
 CC CARBOHYD 124 124
 CC N-linked (GlcNAc...) (Potential).


```
QY 421 RDSPHSERY 429
Db 416 RDSPHSERH 424

RESULT 14
Q35947 PRELIMINARY; PRT; 461 AA.
AC O35947;
DT 01-JAN-1998 (Tremblrel. 05, Created)
DT 01-JAN-1998 (Tremblrel. 05, Last sequence update)
DT 01-MAR-2004 (Tremblrel. 26, Last annotation update)
DE Neuregulin.
OS Mesocricetus auratus (Golden hamster).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Cricetinae;
OC Mesocricetus.
OX NCBI_TaxID=10036;
RN [1]
RP SEQUENCE FROM N.A.
RA Velasco J.A., Feijoo E., Avila M.A., Notario V.;
RL Submitted (APR-1997) to the EMBL/GenBank/DBJ databases.
CC -1- SIMILARITY: Contains 1 EGF-like domain.
DR EMBL; U96612; BAB71812.1; -.
DR HSP; Q12780; IIRE.
DR GO; GO:0005102; F:receptor binding; IEA.
DR GO; GO:0009790; P:embryonic development; IEA.
DR InterPro; IPR000742; EGF 2.
DR InterPro; IPR006209; EGF-like.
DR InterPro; IPR006210; IEGF.
DR InterPro; IPR007110; Ig-like.
DR InterPro; IPR003598; Ig_c2.
DR InterPro; IPR002154; Neuregulin.
DR Pfam; PF00008; EGF; 1.
DR Pfam; PF00047; ig; 1.
DR PRINTS; PR01089; Neuregulin; 1.
DR SMART; SM00181; EGF; 1.
DR SMART; SM00408; IGC2; 1.
DR PROSITE; PS00022; EGF 1; 1.
DR PROSITE; PS01186; EGF 2; 1.
DR PROSITE; PS50026; EGF 3; 1.
DR PROSITE; PS50835; IG_LIKE; 1.
KW EGF-like domain.
SQ SEQUENCE 461 AA; 50890 MW; 935C9560F7148336 CRC64;

Query Match 57.2%; Score 1916; DB 2; Length 461;
Best Local Similarity 86.7%; Pred. No. 2.3e-97;
Matches 373; Conservative 19; Mismatches 30; Indels 8; Gaps 3;

QY 1 MSERKEGRGKGKGGKPPESAGSOSPALPQPKEMKQESAGSKLVLRCTS 60
Db 1 MSERKEGRGKGKGGKPPESAGSOSPALPQPKEMKQESAGSKLVLRCTS 60

QY 61 SEYSSLRPFKFWKNGNELNKNKPNQIKQKPKSELNKLASLADSGYMKVSKLGN 120
Db 61 SEYPELRFKFWKNGSELNKRTPQNIKQKPKSELNKLASLADSGYMKVSKLGN 120

QY 121 DSANITIVESNEITGMPASTGAYVSSSPIRISVSTEGANTSSSTSTSTGTHLV 180
Db 121 DSANITIVDSNEFITGMPASTRAYVSSSPIRISVSTEGANTSSSTSTSTGTHLV 180

QY 181 KCAEKEKTCVNGGECFVKDLSNPRLCKCPNEFTGDRCONVYMASFYKHLGIEFME- 239
Db 181 KCAEKEKTCVNGGECFVKDLSNPRLCKCPNEFTGDRCONVYMASFYKHLGIEFME- 234

QY 240 ABELYQKRVLTITGICALLVVGIMCVAYCKTKQKQKLDRLQSLRSERNNMNIN 299
Db 235 ABELYQKRVLTITGICALLVVGIMCVAYCKTKQKQKLDRLQSLRSERNNMNIN 294

QY 300 GPHHPNPPENVOLNQYVSKNVISSEHIVERAETSFSHTSTTAHSTTVTPPSHS 359
Db 295 GPHHPNPPETVLQVNVQYVSKNIISSSEHIVERAETSFSHTSTTAHSTTVTPPSHS 354
```

```
QY 360 WNGHTESILSHSVVMSVSVNHRSHSPCTGPRGLNGTGGPRECNFLRHARETPDS 419
Db 355 WNGHTESIVSHSVVMSVSVNHRSHSPAGGPRGLHGLGG-LQCNFLRHARETPDS 413

QY 420 YRDSPHSERY 429
Db 414 YRDSPHSERH 423

RESULT 15
Q6TGK9 PRELIMINARY; PRT; 394 AA.
ID Q6TGK9
AC Q6TGK9;
DT 05-JUL-2004 (Tremblrel. 27, Created)
DT 05-JUL-2004 (Tremblrel. 27, Last sequence update)
DT 05-JUL-2004 (Tremblrel. 27, Last annotation update)
DE Neuregulin 1 alpha isoform (Fragment).
OS Oryctolagus cuniculus (Rabbit).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Lagomorpha; Leporidae; Oryctolagus.
OX NCBI_TaxID=9986;
RN [1]
RP SEQUENCE FROM N.A.
RA Hendrickx J.;
RL Submitted (SEP-2003) to the EMBL/GenBank/DBJ databases.
CC -1- SIMILARITY: Contains 1 EGF-like domain.
DR EMBL; AY421758; AAR00250.1; -.
DR GO; GO:0005102; F:receptor binding; IEA.
DR GO; GO:0009790; P:embryonic development; IEA.
DR InterPro; IPR000742; EGF 2.
DR InterPro; IPR006209; EGF-like.
DR InterPro; IPR006210; IEGF.
DR InterPro; IPR003599; Ig.
DR InterPro; IPR007110; Ig-like.
DR InterPro; IPR003598; Ig_c2.
DR InterPro; IPR002154; Neuregulin.
DR Pfam; PF00008; EGF; 1.
DR Pfam; PF00047; ig; 1.
DR PRINTS; PR01089; Neuregulin; 1.
DR SMART; SM00181; EGF; 1.
DR SMART; SM00409; IG; 1.
DR SMART; SM00408; IGC2; 1.
DR PROSITE; PS00022; EGF 1; 1.
DR PROSITE; PS01186; EGF 2; 1.
DR PROSITE; PS50026; EGF 3; 1.
DR PROSITE; PS50835; IG_LIKE; 1.
KW EGF-like domain.
FT NON_TER 1
FT NON_TER 394
SQ SEQUENCE 394 AA; 42980 MW; C183EB80927443F9 CRC64;

Query Match 56.0%; Score 1875.5; DB 2; Length 394;
Best Local Similarity 91.7%; Pred. No. 3.2e-95;
Matches 366; Conservative 6; Mismatches 22; Indels 5; Gaps 1;

QY 10 KKGKKKGGKGGKPPESAGSOSPALPQPKEMKQESAGSKLVLRCTSSEYSSLRPK 69
Db 1 KKGKKKGGKGGKPPADGGPSPALPRLKEMKQESAGSKLVLRCTSSEYSSLRPK 60

QY 70 WFKNGNELNKNKPNQIKQKPKSELNKLASLADSGYMKVSKLGNDSANIT 129
Db 61 WFKNGNELNKNKPNQIKQKPKSELNKLASLADSGYMKVSKLGNDSANIT 120

QY 130 VESNEIITGMPASTGAYVSSSPIRISVSTEGANTSSSTSTSTGTHLVKCAEKEKTF 189
Db 121 VESNEIITGMPASTRAYVSSSPIRISVSTEGANTSSSTSTSTGTHLVKCAEKEKTF 180

QY 190 CVNGGECFVKDLSNPRLCKCPNEFTGDRCONVYMASFYKHLGIEFMEABELYQKRV 249
Db 181 CVNGGECFVKDLSNPRLCKCPNEFTGDRCONVYMASFYKHLGIEFMEABELYQKRV 235
```

```
QY 250 TITGICIALLVGIMCWAYCKTKQKQKLDRLQSLRSERNMMNIANGPHHPPE 309
    |||||:|||||
Db 236 TITGICIALLVGIMCWAYCKTKQKQKLDRLQSLRSERNMMNIANGPHHPPE 295
    |||||:|||||
QY 310 NVOLNQYVSKNVISSEHIVEREAETSFSTSHYTSTAHHSTTQTTPSHWSNGHTESIL 369
    |||||:|||||
Db 296 NVOLNQYVSKNVISSEHIVEREAETSFSTSHYTSTAHHSTTQTTPSHWSNGHTESII 355
    |||||:|||||
QY 370 SESHVIMSSVENSSEHSSPTGGPRGLNGTGGPRECNS 408
    |||||:|||||
Db 356 SESHVIMSSVENSSEHSSPTGGPRGLNGLGGPRECNS 394
    |||||:|||||
```

Search completed: April 12, 2005, 14:33:51
Job time : 187 secs

GenCore version 5.1.6
Copyright (c) 1993 - 2005 CompuGen Ltd.

OM protein - protein search, using sw model

Run on: April 12, 2005, 14:26:42 ; Search time 48 Seconds
(without alignments)
1292.913 Million cell updates/sec

Title: US-10-082-747A-93
Perfect score: 3347
Sequence: 1 MSERKEGKGKGGKKGKRGSS.....QBEIQARLSSVIANQDPIAV 645
Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 283416 seqs, 96216763 residues
Total number of hits satisfying chosen parameters: 283416

Minimum DB seq length: 0
Maximum DB seq length: 2000000000
Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : PIR 79:*
1: pir1:*
2: pir2:*
3: pir3:*
4: pir4:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	ID	Description
1	3343	99.9	645	B43273	herregulin, splice
2	3280	98.0	637	C43273	herregulin, precursor
3	3202.5	95.7	640	A43273	herregulin, precursor
4	3066.5	91.6	636	I61718	neu differentiation
5	3058.5	91.4	662	I61722	neu differentiation
6	2980	89.0	639	I61719	neu differentiation
7	2526.5	75.5	602	A45769	acetylcholine rece
8	2086.5	62.3	462	I38404	neu differentiation
9	1751.5	52.3	350	I38403	neu differentiation
10	1183	35.3	241	D43273	herregulin, precursor
11	1098	32.8	241	S32359	glial growth facto
12	1059	31.6	230	A56210	neu differentiation
13	1028	30.7	868	JC5701	ErbB kinase activa
14	993	29.7	850	JC5700	ErbB kinase activa
15	982	29.6	860	JC5702	ErbB kinase activa
16	827	24.7	422	S32357	glial growth facto
17	788	23.5	175	I38408	neu differentiation
18	545.5	16.3	125	S62676	herregulin isoform
19	485	14.5	125	I38405	neu differentiation
20	351	10.5	296	A56943	sensory/motor neur
21	334.5	10.0	713	T44447	neuregulin-3 (impo
22	182.5	5.5	57	PC4415	ErbB kinase activa
23	181	5.4	2254	D86215	protein T6D22.14 l
24	179	5.3	3507	T34513	hypothetical prote
25	172	5.1	734	B42680	nucleolus-cytoplas
26	171	5.1	1091	IJCHNL	neural cell adhesi
27	170	5.1	1891	T13594	hypothetical prote
28	169	5.0	1920	T13893	gene handsight pro
29	161	4.8	1510	T33100	hypothetical prote

30	159	4.8	1192	2	T18611	probable serine/th
31	157	4.7	6642	2	T29757	protein UNC-89 - C
32	156.5	4.7	279	2	T16201	hypothetical prote
33	155.5	4.6	1306	2	S25370	MSB2 protein - yea
34	151.5	4.5	955	2	E84845	probable villin 2
35	151.5	4.5	7962	2	I38346	elastic titin - hu
36	151	4.5	5327	2	T13564	microtubule-associ
37	150	4.5	1092	1	JN0635	neural cell adhesi
38	149.5	4.5	1367	2	S74285	BUD3 protein - yea
39	149	4.5	409	2	S70704	carbon catabolite
40	149	4.5	1271	2	T24008	hypothetical prote
41	147.5	4.4	699	2	I38073	nucleolar phosphop
42	147	4.4	1203	2	T17415	mycellial surface a
43	146.5	4.4	402	2	E86185	hypothetical prote
44	146.5	4.4	844	2	S61112	regulatory protein
45	146	4.4	534	2	T39903	serine-rich protei

ALIGNMENTS

RESULT 1

B43273
herregulin, splice form beta 1 - human
C:Species: Homo sapiens (man)
C:Date: 31-Dec-1993 #sequence_revision 31-Dec-1993 #text_change 09-Jul-2004
C:Accession: B43273; I38406
R:Holmes, W.E.; Sliwkowski, M.X.; Akita, R.W.; Henzel, W.J.; Lee, J.; Park, J.W.; Yansu
Science 256, 1205-1210, 1992
A:Title: Identification of herregulin, a specific activator of p185(erbB2).
A:Reference number: A43273; MUID:92271253; PMID:1350381
A:Accession: B43273
A:Status: preliminary; nucleic acid sequence not shown; not compared with conceptual tr.
A:Molecule type: mRNA
A:Residues: 1-645 <HOL>
A:Cross-references: UNIPROT:Q02297
R:Wen, D.; Suggs, S.V.; Karunakaran, D.; Liu, N.; Cupples, R.L.; Luo, Y.; Janssen, A.M.,
Mol. Cell. Biol. 14, 1909-1919, 1994
A:Title: Structural and functional aspects of the multiplicity of Neu differentiation f
A:Reference number: A56210; MUID:94158863; PMID:7509448
A:Accession: I38406
A:Status: preliminary; translated from GB/EMBL/DBJ
A:Molecule type: mRNA
A:Residues: 'A', 95-418, 'F', 420-645 <RES>
A:Cross-references: EMBL:U02328; NID:G408406; PIDN:AAA19953.1; PID:G408407
C:Genetics:
A:Gene: GDB:HGL
A:Cross-references: GDB:I32656; OMIM:142445
A:Map position: 8p22-8p11
C:Superfamily: human herregulin; EGF homology; immunoglobulin homology
C:Keywords: alternative splicing
F:182-221/Domain: EGF homology <EGF>

Query Match 99.9%; Score 3343; DB 2; Length 645;
Best Local Similarity 99.8%; Pred. No. 1.3e-183;
Matches 644; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY	1	MSERKEGKGKGGKKGKRGSSQSPALPPOLKEMKSOESAAAGSKLVLRCE	60
DB	1	MSERKEGKGKGGKKGKRGSSQSPALPPOLKEMKSOESAAAGSKLVLRCE	60
QY	61	SEYSSILRPFKWFNGNGLNKNKPNQIKIQKPGKSELINKASLADSGEYMCVKV	120
DB	61	SEYSSILRPFKWFNGNGLNKNKPNQIKIQKPGKSELINKASLADSGEYMCVKV	120
QY	121	DSASANTITVESNEIITGMPASTEGAYVSSSEPIRISVSTEGANTSSSTSTT	180
DB	121	DSASANTITVESNEIITGMPASTEGAYVSSSEPIRISVSTEGANTSSSTSTT	180
QY	181	KCAEKEKTCVNGGCFWVKDLSNPSRYLCKCPNEFTGDRCONYVWASFYKHLG	240
DB	181	KCAEKEKTCVNGGCFWVKDLSNPSRYLCKCPNEFTGDRCONYVWASFYKHLG	240

Qy	241	EELYQKRVLTITGICITALLVVGIMCVVAYCKTKQKQKGLHDLRQSLRGERNNMMNIANG	300
Db	241	EELYQKRVLTITGICITALLVVGIMCVVAYCKTKQKQKGLHDLRQSLRGERNNMMNIANG	300
Qy	301	PHHPNPPENVOLVNOQVSVKNVTSSEHIVERAEATSFSTSHYTSTAHHSTTVTTQTPSHW	360
Db	301	PHHPNPPENVOLVNOQVSVKNVTSSEHIVERAEATSFSTSHYTSTAHHSTTVTTQTPSHW	360
Qy	361	SNGHTEILSESHSVIWMSSVENSRRHSSPTGGPRGRLNGTGGPRECNCSFLRHARETPDSY	420
Db	361	SNGHTEILSESHSVIWMSSVENSRRHSSPTGGPRGRLNGTGGPRECNCSFLRHARETPDSY	420
Qy	421	RDSPHSERYVSAMTTTPARMSPVDFHTPSSPKSPFSEMSPPVSSMTVSMPSMAVSPWEESE	480
Db	421	RDSPHSERYVSAMTTTPARMSPVDFHTPSSPKSPFSEMSPPVSSMTVSMPSMAVSPWEESE	480
Qy	481	RPLLLVTPPLRKKFDHPHQOQSSPHHNPAHNSLNPASPLRIVDEDEYETTQYEYPAQ	540
Db	481	RPLLLVTPPLRKKFDHPHQOQSSPHHNPAHNSLNPASPLRIVDEDEYETTQYEYPAQ	540
Qy	541	EPVKKLANSRRARKTPNGHIANRLEVDNSTSQSSNSESETERDVGEDTTPFLGIQNPL	600
Db	541	EPVKKLANSRRARKTPNGHIANRLEVDNSTSQSSNSESETERDVGEDTTPFLGIQNPL	600
Qy	601	AASLEATPAFLADSRTPNAGRFSTQEEIQARLSSVIANQDPIAV	645
Db	601	AASLEATPAFLADSRTPNAGRFSTQEEIQARLSSVIANQDPIAV	645

RESULT 2
 C43273
 heregulin precursor, splice form beta-2 - human
 C:Species: Homo sapiens (man)
 C:Date: 31-Dec-1993 #sequence_revision 31-Dec-1993 #text_change 08-Sep-2002
 C:Accession: C43273; I38407
 R:Holmes, W.E.; Sliwkowski, M.X.; Akita, R.W.; Henzel, W.J.; Lee, J.; Park, J.W.; Yansu
 Science 256, 1205-1210, 1992
 A:Title: Identification of heregulin, a specific activator of p185(erbB2).
 A:Reference number: A43273; MUID:92271263; PMID:1350381
 A:Accession: C43273
 A>Status: preliminary; nucleic acid sequence not shown; not compared with conceptual tra
 A:Molecule type: mRNA
 A:Residues: 1-637 <HOL>
 R:Wen, D.; Suggs, S.V.; Karunakaran, D.; Liu, N.; Cupples, R.L.; Luo, Y.; Janssen, A.M.;
 Mol. Cell. Biol. 14, 1909-1919, 1994
 A:Title: Structural and functional aspects of the multiplicity of Neu differentiation fa
 A:Reference number: A56210; MUID:94158863; PMID:7509448
 A:Accession: I38407
 A>Status: preliminary; translated from GB/EMBL/DBJ
 A:Molecule type: mRNA
 A:Residues: 119-406 <RES>
 A:Cross-references: EMBL:U02329; NID:g408408; PIDN:AAA19954.1; PID:g408409
 C:Genetics:
 A:Gene: GDB:HGL
 A:Cross-references: GDB:132656; OMIM:142445
 A:Map position: 9p22-8p11
 C:Superfamily: human heregulin; EGF homology; immunoglobulin homology
 C:Keywords: alternative splicing
 F:182-221/Domain: EGF homology <EGF>

Query Match 98.0%; Score 3280; DB 2; Length 637;
 Best Local Similarity 98.4%; Pred. No. 5,1e-180;
 Matches 635; Conservative 1; Mismatches 1; Indels 8; Gaps 1;

Qy	1	MSRKKEGRGKGKKGKGGKGPESAGSQSPALPPQLKEMKQSBSAAGSKLVLRCTS	60
Db	1	MSRKKEGRGKGKKGKGGKGPESAGSQSPALPPRLKEMKQSBSAAGSKLVLRCTS	60
Qy	61	SEYSSSLFQKFGKNGELNRKNKQNIKIQKPKGSELINKASLADSGEYMWCKVSKLGN	120
Db	61	SEYSSSLFQKFGKNGELNRKNKQNIKIQKPKGSELINKASLADSGEYMWCKVSKLGN	120
Qy	121	DSASANITIVESNELITGMPASTEGAYVSVSESPRISVSTEGANTSSSTSTSTTGTGSHLV	180

C; Keywords: alternative splicing; glycoprotein
F:182-221/Domain: EGF homology <EGF>

Query Match	95.7%	Score 3202.5;	DB 2;	Length 640;
Best Local Similarity	96.7%	Pred. No. 1.4e-175;		
Matches 624:	Conservative	1;	Mismatches 15;	Indels 5;
				Gaps 1;

Qy	1	MSEKEGRGKGKGGKKERGSGKKPESAAAGSOSPALPPOLKEMKSQESAAGSKLVLRCE	60
Dδ	1	MSEKEGRGKGKGGKKERGSGKKPESAAAGSOSPALPPOLKEMKSQESAAGSKLVLRCE	60

Qy	61	SEYSLRFKWFQNGNELNRKNKPONTIKIOKPGKSELRNKA SLADSGEYMCKVISKIGN	120
Db	61	SEYSLRFKWFQNGNELNRKNKPONTIKIOKPGKSELRNKA SLADSGEYMCKVISKIGN	120

[illegible][illegible]

Qy	241	BELYOKRVLTITGICIAALLVVGIMCVWAYCKTKORKKLUHDLRQSLRSERNMMNIANG	300
<div style="height: 1em; background-color: black;"></div>			
Db	236	EELYOKRVLTITGICIAALLVVGIMCVWAYCKTKORKKLUHDLRQSLRSERNMMNIANG	295

Qy	301	PHHPNPPPNVQLNVQYVKNVISSEHI VEREAETSFSTSHYSTTAHHSTTTVTOTPSHSW	360
Db	296	PHHPNPPPNVQLNVQYVKNVISSEHI VEREAETSFSTSHYSTTAHHSTTTVTOTPSHSW	355

Qy	361	SNGHTEILSEHSVIVMSSVENSRRSSPTGGPRGLNGTGGPRECNFLRHARETPDSY	420
Dδ	356	SNGHTEILSEHSVIVMSSVENSRRSSPTGGPRGLNGTGGPRECNFLRHARETPDSY	415

Qy	421	RDSHSERYVSAMTTPARMSPVDFHTFPSSPKSPPEMSPVSVMTVSNPMSVAVSPWEEEE	480
Db	416	RDSHSERYVSAMTTPARMSPVDFHTFPSSPKSPPEMSPVSVMTVSNPMSVAVSPWEEEE	475

Qy	481	RPLLLVTPRLREKKFDHHPQOFSSFHNPANHSNLSASPPLRIVEDEEYEYTOQEYPAQ	540
<hr/>			
Db	476	RPLLLVTPRLREKKFDHHPQOFSSFHNPANHSNLSASPPLRIVEDEEYEYTOQEYPAQ	535

Qy	541	EPVKLANRRAR ^K T ^K KN ^G HIANRLEVDNSTSSQSSNSSSETEDERVGEDT ^F LGIQNPL 600
Db	536	EPVKLANRRAR ^K T ^K KN ^G HIANRLEVDNSTSSQSSNSSSETEDERVGEDT ^F LGIQNPL 595

[illegible]

RESULT 4
I61718

C; Species: Rattus norvegicus (Norway rat)
C; Date: 29-May-1998 #sequence: revision 29-May-1998 #text_change 09-Jul-2004
C; Accession: I61718; I61721; I61720
R; Wen, D.; Suggs, S.V.; Karunakaran, D.; Liu, N.; Cupples, R.L.; Luo, Y.; Janssen, A.M.;
Mol. Cell. Biol. 14, 1909-1919, 1994
A; Title: Structural and functional aspects of the multiplicity of Neu differentiation fa
A; Reference number: A56210; MUID: 94158863; PMID: 7509448

A;Status: preliminary; translated from GB/EMBL/DBDJ
A;Molecule type: mRNA
A;Residues: 1-636 <RES>
A;Cross-references: UNIPROT:P43322; EMBL:U02318; NID:G408386; PIDN:AAAL19943.1; PID:G408393
A;Accession: I61720
A;Status: preliminary; translated from GB/EMBL/DBDJ
A;Molecule type: mRNA
A;Residues: 1-444, 'A', 446-636 <RE2>
A;Cross-references: EMBL:U02321; NID:G408392; PIDN:AAAL19946.1; PID:G408393
A;Accession: I61720

A;Status: preliminary; translated from GB/EMBL/DBD
A;Molecule type: mRNA
A;Residues: 1-298,386, 'V',388, 'TR',391, 'RE3'
A;Cross-references: EMBL:U02320; NID:G408390; PIDN:AA119945.1; PID:G408391
C;Superfamily: human heregulin; EGF homology;
F:182-221/Domain: EGF homology
F:182-221/Domain: EGF homology

Query Match	91.6%	Score 3066.5;	DB 2;	Length 636;
Best Local Similarity	91.6%;	Pred. No. 8e-168;		
Matches 591:	Conservative	22;	Mismatches 23;	Indels 9;
Gaps				

Qy	1	MSERKEBGRGKGKKKRGSGKKKPESAAAGSQSPALPPOLKEMKSKQESAAAGSKLVLRCTS	60
		MSERKEBGRGKGKKKRGSGKKKPESAAAGSQSPALPPOLKEMKSKQESAAAGSKLVLRCTS	60
Dp	1	MSERKEBGRGKGKKKRGSGRGGPAAEGDPSALPPRLKEMKSKQESAAAGSKLVLRCTS	60
		MSERKEBGRGKGKKKRGSGRGGPAAEGDPSALPPRLKEMKSKQESAAAGSKLVLRCTS	60

[illegible]

Qy	121	DSASANTIV	ESNEIITG	MPASTEGA	VYSS	ESPIRISV	STEGANT	SSSTSTST	TGTGSHLV	180
Dd	121	DSASANTIV	ESNEFIIC	MPASTETA	VYSS	ESPIRISV	STEGANT	SSSTSTST	TGTGSHLI	180

Qy	181	KCAEKEKTFCVNGGECFTVKVQLSNPSRYLCKCPNEFTGDRCQNYVMASFYKHGLGFMEB	240
Db	181	KCAEKEKTFCVNGGECFTVKVQLSNPSRYLCKCPNEFTGDRCQNYVMASFYK-----A	232

Qy	241	EELYQKRVLTITGICIALLVGIMCVAYCKTKQKQKLDHRLQSLRSERNMMNIANG	300
Db	233	EELYQKRVLTITGICIALLVGIMCVAYCKTKQKQKLDHRLQSLRSERNLVNIANG	292

Qy	301	PHHPNP	PEN	VL	NO	VY	SK	NO	VI	SE	HI	VE	RE	AE	TS	SH	YT	ST	TA	HH	ST	VT	QT	PS	HW	360
Db	293	PHHPNP	PEN	VL	NO	VY	SK	NO	VI	SE	HI	VE	RE	VE	TS	SH	YT	ST	TA	HH	ST	VT	QT	PS	HW	352

Qy	361	SNHGTEILSESHSVIWMSSVENSRRHSSTGGPRGRNLNGTGGPRECSNGLRHARETPDSY	420
Dp	353	SNHGTESVISENSVIWMSSVENSRRHSSTGGPRGRHLGLGGPRD-NSFLRHARETPDSY	411

Qy	421	RDSPHSRYVSAMTT	PARMS	PVD	FHT	PS	PK	SP	PP	SE	MS	PP	V	S	M	T	V	S	M	P	S	M	A	V	S	P	F	M	E	E	480
Db	412	RDSPHSRYVSAMTT	PARMS	PVD	FHT	PS	PK	SP	PP	SE	MS	PP	V	S	M	T	V	S	M	P	S	M	A	V	S	P	F	M	E	E	471

Qy	481	RP	LL	LV	PP	RL	RE	KK	F	D	H	H	P	Q	F	S	F	F	H	N	P	A	D	S	N	S	L	P	A	S	P	L	R	I	V	E	D	E	E	E	Y	T	T	Q	E	Y	P	A	Q	540
D6	472	RP	LL	LV	PP	RL	RE	KK	F	D	H	H	P	Q	F	S	F	F	H	N	P	A	D	S	N	S	L	P	A	S	P	L	R	I	V	E	D	E	E	E	Y	T	T	Q	E	Y	P	A	Q	531

[illegible][illegible]

```

RESULT 5
161722
neu differentiation factor - rat
C:Species: Rattus norvegicus (Norway rat)
C:Date: 29-May-1998 #sequence_revision 25-May-1998 #text_change 09-Jul-2004
C:Accession: I61722
R:Wen, D.; Suggs, S.V.; Karunakaran, D.; Liu, N.; Cupples, R.L.; Luo, Y.; Janssen, J.
Mol. Cell. Biol. 14, 1909-1919, 1994
A:Title: Structural and functional aspects of the multiplicity of Neu differentiation factor
A:Reference number: A56210; MUID:94158863; PMID:7509448
A:Accession: I61722
A:Status: preliminary; translated from GE/EMBL/DBDJ
A:Molecule type: mRNA
A:Residues: 1-662 <RES>
A:Cross-references: UNIPROT:P43322; EMBL:U02322; NID:G408394; PIDN:AAA19947.1;
C:Superfamily: human heregulin; EGF homology; immunoglobulin homology
P:182-321/Domain: EGF homology <EGF>

```


Db 594 LAASLEVAPAFRLAESRTNPAGRFSTOEELOARLSSVIANODPIAV 639

RESULT 7

A45769
acetylcholine receptor synthesizes stimulator ARIA-1 precursor - chicken
C:Species: Gallus gallus (chicken)
C:Date: 20-Feb-1995 #sequence_revision 20-Feb-1995 #text_change 09-Jul-2004
C:Accession: A45769
R:Fallis, D.L.; Rosen, K.M.; Corfas, G.; Lane, W.S.; Fischbach, G.D.
Cell 72, 801-815, 1993
A:Title: ARIA, a protein that stimulates acetylcholine receptor synthesis, is a member
A:Reference number: A45769; MUID:93201602; PMID:8453670
A:Accession: A45769
A:Status: preliminary
A:Molecule type: mRNA; protein
A:Residues: 1-602 <PAL>
A:Cross-references: UNIPROT:Q05199; GB:L11264; NID:G212603; PID:AAA49037.1; PID:G212604
A:Experimental source: brain
A:Note: sequence extracted from NCBI backbone (NCBIN:127787, NCBIP:127788)
C:Superfamily: human heregulin; EGF homology; immunoglobulin homology

Query Match	75.5%; Score 2526.5; DB 2; Length 602;
Best Local Similarity	77.2%; Pred. No. 5.3e-137;
Matches	480; Conservative 54; Mismatches 51; Indels 37; Gaps 4;
QY	25 ESAAGSQSPALPOLKEMKSOESAAGSKULVLCETSEYSSLRPFKFKNGNELNKKVKQ 84
DB	17 QTDVNSYNTVPKPKEMKNQEVAGQGLVLCETTSYPALEFRKWLKNGKEITKNRPE 76
QY	85 NIKIOKKPGK-SELRLNKASLADSGYMKCVKISLGNDSASANITIVESNEIITGMPAST 143
DB	77 NVKIPKQKYSSELHYIRATLADAGYACRVSSKLGNDSTKASVIITDN----- 126
QY	144 EGAYVSSSESPIRISVSTEGANTSSSTSTSTGTSHLVKCAEKEKTECVANGGECFMVKOLS 203
DB	127 -----ATSTSTGTSHLTKCDIKQKACVANGGECYMKDLP 162
QY	204 NPSRYLCKPNEBTGDRCONYMASPYKHLGIEFMEABELYQKRVLTITGICIALLVGI 263
DB	163 NPPLYLRCPCNEBTGDRCONYMASPYKHLGIEFMEABELYQKRVLTITGICIALLVGI 222
QY	264 MCVVAYCKTKQKOKKLDRLROSLRERNMMNIANGPHHPNPPPNVOLVNOQYVSKNVI 323
DB	223 MCVVAYCKTKQKOKKLDRLROSLRERNMMNIANGPHHPNPPPNVOLVNOQYVSKNII 282
QY	324 SSEHIVVERAETSFSSTHYTSTAHHSTTTTQTPSHWSNGHTESILSESHVIVMSSVEN 383
DB	283 SSERVVERETSFSTSHYSTTHHSMTVTQTPSHWSNGHTESILSESHVIVMSSVEN 342
QY	384 SRHSSSTGPRGLNLTGTPRECNSFLRHARETTPDSYRSPHSERYVSAWTTTARMSPVD 443
DB	343 SRHTSPT-GPRGLNLTGTPRECNSFLRHARETTPDSYRSPHSERYVSAWTTTARMSPVD 401
QY	444 FHTPSPKPPSPMSPPVSMVTVMSPMAVSPMEERPLLIVTPRLBEKFDHHQPOF 503
DB	402 FHTPSPKPPSPMSPPVSSLTISISVAVSPPMDEERPLLIVTPRLRE-KYDNLHQF 460
QY	504 SGPHPNPAHDSNLPASPLRIVEDEYEYTOEYEPAQEPVKLANRRRAKTRKPNGHIAN 563
DB	461 NSFHPNPTSHSNLPPSPLRIVEDEYEYTOEYEPAQEPVKLTNSRRVRYKPNGHISS 520
QY	564 RLEVDNNTSSQSNSSSETEDERVGDDTFLPGLQNPPLAASLEATPAFLADSRTPNAGR 623
DB	521 RVEVDSDTSSQSTSSSETEDERIGDTPFLSLQNPWATSLRPAAYRLAENRTNPANRF 580
QY	624 STQEELQARLSSVIANQDPIAV 645
DB	581 STPEELQARLSSVIANQDPIAV 602

SECRET

RESOL
I38404

neu differentiation factor - human

C;Species: Homo sapiens (man)
C;Date: 29-May-1998 #sequence_revision 29-May-1998 #text_change 09-Jul-2004
C;Accession: I38404
R;Men, D.; Suggs, S. V.; Karungaran, D.; Liu, N.; Cupples, R.L.; Luo, Y.; Janssen, A.M.
Mol. Cell. Biol. 14, 1909-1919, 1994
A;Title: Structural and functional aspects of the multiplicity of Neu differentiation f
A;Reference number: A56210; MUID:94158863; PMID:7509448
A;Accession: I38404
A;Status: preliminary; translated from GB/EMBL/DBJ
A;Molecule type: mRNA
A;Residues: 1-462 <RES>
A;Cross-references: UNIPROT:Q02297; EMBL:U02326; NID:g408402; PIDN:AAA19951.1; PID:g408
C;Superfamily: human heregulin; EGF homology; immunoglobulin homology

Query Match	62.3%	Score 2086.5	DB 2	Length 462
Best Local Similarity	94.6%	Pred. No. 5.2e-112		
Matches	406	Conservative	3	Mismatches 15; Indels 5; Gaps 1;
Qy	1	MSRKEGRGKGKKKVERGSGKPPESAAQSQSPALPPQLKEMKQESAAGSKVLVRCBTS	60	
Db	1	MSRKEGRGKGKKKVERGSGKPPESAAQSQSPALPPRLKEMKQESAAGSKVLVRCBTS	60	
Qy	61	SEYSSLRFRKFKNGNELNRKNKPNIKIQKPKGKSELRINKASLADSGEYMKVSKLGN	120	
Db	61	SEYSSLRFRKFKNGNELNRKNKPNIKIQKPKGKSELRINKASLADSGEYMKVSKLGN	120	
Qy	121	DSASANITIVESNEIITGMPASTEGAYVSSSPRISVSTEGANTSSTSTSTTGTSHLV	180	
Db	121	DSASANITIVESNEIITGMPASTEGAYVSSSPRISVSTEGANTSSTSTSTTGTSHLV	180	
Qy	181	KCAEKEKTFVCVNGGECFVWKDLNPSRYLCKCPNEFTGDRCONVYMASFYKHLGIEFMFA	240	
Db	181	KCAEKEKTFVCVNGGECFVWKDLNPSRYLCKCPGFTGARCTENVPMKVQOQ----	235	
Qy	241	EELYQRVLVITIGICITALLVVGIMCVAYCTKKQRKLDHRLRQSLRSENNMMNIANG	300	
Db	236	EELYQRVLVITIGICITALLVVGIMCVAYCTKKQRKLDHRLRQSLRSENNMMNIANG	295	
Qy	301	PHPNPPPPENVQLVNOVSVKNVLSSEHIVERAETSFSHYTSTAHHSTTVTQTPSHSW	360	
Db	296	PHPNPPPPENVQLVNOVSVKNVLSSEHIVERAETSFSHYTSTAHHSTTVTQTPSHSW	355	
Qy	361	SNHGTSILSESHSVIWMSSVENSRHSSPTGGPRGRNLNGTGGPRECNFLRHARETPDSY	420	
Db	356	SNHGTSILSESHSVIWMSSVENSRHSSPTGGPRGRNLNGTGGPRECNFLRHARETPDSY	415	
Qy	421	RDSPHSERY	429	
Db	416	RDSPHSERH	424	

RESIST. 9

new differentiation factor - human (fragment)
 C:Species: Homo sapiens (man)
 C:Date: 29-May-1998 #sequence_revision 29-May-1998 #text_change 08-Sep-2002
 C:Accession: I38403
 R;Wen, D.; Suggs, S.V.; Karunakaran, D.; Liu, N.; Cupples, R.L.; Luo, Y.; Janssen, A.M.
 Mol. Cell. Biol. 14, 1909-1919, 1994
 A:Title: Structural and functional aspects of the multiplicity of Neu differentiation f
 A:Reference number: A56210; MUID:94158863; PMID:7509448
 A:Accession: I38403
 A:Status: preliminary; translated from GB/EMBL/DBDJ
 A:Molecule type: mRNA
 A:Residues: 1-350 <RES>
 A:Cross-references: EMBL:U02325; NID:G408400; PIDN:AAA19950.1; PID:G408401
 C:Superfamily: human heregulin; EGF homology; immunoglobulin homology

Query Match 52.3%; Score 1751.5; DB 2; Length 350;
Best Local Similarity 95.1%; Pred. No. 5.1e-93;
Matches 333; Conservative 4; Mismatches 10; Indels 3; Gaps 1;

QY 194 GECFMVKDLSNPSRYLCKPNEFTGDRCONVY----MASFYKHLGIFMEABELYQKRVLT 250
Db 1 GECFMVKDLSNPSRYLCKPNEFTGDRCONVY----MASFYKHLGIFMEABELYQKRVLT 60
QY 251 ITGICITALLVVGIMCVVAYCKTKQKRLHDLRLQSLRERNMMNIANGPHHPNPPEN 310
Db 61 ITGICITALLVVGIMCVVAYCKTKQKRLHDLRLQSLRERNMMNIANGPHHPNPPEN 120
QY 311 VOLVNOYVSKNVISSHHIVERAEFTSFSHTSTTAHSTTTVOTPSHSWSNGHTESILS 370
Db 121 VOLVNOYVSKNVISSHHIVERAEFTSFSHTSTTAHSTTTVOTPSHSWSNGHTESILS 180
QY 371 EHSVIVMSVSVNRSRHSPTGPRGLNGTGPRECNSFLRHARETDSYRDSPSHSERV 430
Db 181 EHSVIVMSVSVNRSRHSPTGPRGLNGTGPRECNSFLRHARETDSYRDSPSHSERV 240
QY 431 SAMTTPARMSVDFTHTPSSPKPPSPMSPPVSMVTVMSPMAVSPPMESERPLLVTTPR 490
Db 241 SAMTTPARMSVDFTHTPSSPKPPSPMSPPVSMVTVMSPMAVSPPMESERPLLVTTPR 300
QY 491 LREKFDHHPQPFSSPHNPAHDSNLSPLRIVEDREYETTOYEPAP 540
Db 301 LREKFDHHPQPFSSPHNPAHDSNLSPLRIVEDREYETTOYEPAP 350

RESULT 10

D43273
heregulin precursor, splice form beta-3 - human
N;Alternate names: glial growth factor HRG-beta-3; neuregulin
C;Species: Homo sapiens (man)
C;Date: 31-Dec-1993 #sequence_revision 31-Dec-1993 #text_change 09-Jul-2004
C;Accession: D43273; S32358
R;Holmes, W.E.; Sliwkowski, M.X.; Akita, R.W.; Henzel, W.J.; Lee, J.; Park, J.W.; Yansui
Science 356, 1205-1210, 1992
A;Title: Identification of heregulin, a specific activator of p185(erbB2).
A;Reference number: A43273; MUID:92271253; PMID:1350381
A;Accession: D43273
A;Status: preliminary; nucleic acid sequence not shown; not compared with conceptual tra
A;Molecule type: mRNA
A;Residues: 1-241 <HOL>
A;Cross-references: UNIPROT:Q02297
R;Marchionni, M.A.; Goodearl, A.D.J.; Chen, M.S.; Bermingham-McDonogh, O.; Kirk, C.; Hen
les, I.; Davis, J.B.; Hsuan, J.J.; Totty, N.F.; Otsu, M.; McBurney, R.N.; Waterfield, M.
Nature 362, 312-318, 1993
A;Title: Glial growth factors are alternatively spliced erbB2 ligands expressed in the n
A;Reference number: S32357; MUID:93205115; PMID:8096067
A;Accession: S32358
A;Molecule type: mRNA
A;Residues: 1-241 <MAR>
A;Cross-references: GB:L12261; NID:9292049; PIDN:AAB59358.1; PID:g292050
C;Genetics:
A;Gene: GDB:HGL; GGF
A;Map position: GDB:132656; OMIM:142445
A;Map position: 8p22-8p11
C;Superfamily: human heregulin; EGF homology; immunoglobulin homology
C;Keywords: alternative splicing
F:182-221/Domain: EGF homology <EGF>

Query Match 35.3%; Score 1183; DB 2; Length 241;
Best Local Similarity 99.6%; Pred. No. 9.6e-61;
Matches 229; Conservative 1; Mismatches 0; Indels 0; Gaps 0;
QY 1 MSERKEGRGKGKKGKRGSGKPSAAGSQSPALPPOLKEMKSOESAAGSKLVLRCTSS 60
Db 1 MSERKEGRGKGKKGKRGSGKPSAAGSQSPALPPOLKEMKSOESAAGSKLVLRCTSS 60
QY 61 SEYSSLRPFKFWKGNELNRKNKPQNIKIQKPGKSELINKASLADSGEYMKVSKLGN 120
Db 61 SEYSSLRPFKFWKGNELNRKNKPQNIKIQKPGKSELINKASLADSGEYMKVSKLGN 120
QY 121 DSANITIVESNEITGMPASTEGAYVSSSPRISVSTEGANTSSSTSTSTTGTSHLV 180
Db 121 DSANITIVESNEITGMPASTEGAYVSSSPRISVSTEGANTSSSTSTSTTGTSHLV 180

QY 181 KCAEKEKTFVNGGECFMVKDLSNPSRYLCKPNEFTGDRCONVYMASFY 230
Db 181 KCAEKEKTFVNGGECFMVKDLSNPSRYLCKPNEFTGDRCONVYMASFY 230
RESULT 11
S32359
glial growth factor - bovine
C;Species: Bos primigenius taurus (cattle)
C;Date: 19-Mar-1997 #sequence_revision 01-Aug-1997 #text_change 09-Jul-2004
C;Accession: S32359
R;Marchionni, M.A.; Goodearl, A.D.J.; Chen, M.S.; Bermingham-McDonogh, O.; Kirk, C.; Hen
les, I.; Davis, J.B.; Hsuan, J.J.; Totty, N.F.; Otsu, M.; McBurney, R.N.; Waterfield, M.
Nature 362, 312-318, 1993
A;Title: Glial growth factors are alternatively spliced erbB2 ligands expressed in the n
A;Reference number: S32357; MUID:93205115; PMID:8096067
A;Accession: S32359
A;Status: preliminary
A;Molecule type: mRNA
A;Residues: 1-241 <MAR>
A;Cross-references: UNIPROT:Q07112; GB:L12259; NID:g289413; PIDN:AAA30540.1; PID:g289414
C;Superfamily: human heregulin; EGF homology; immunoglobulin homology
F:182-221/Domain: EGF homology <EGF>

Query Match 32.8%; Score 1098; DB 2; Length 241;
Best Local Similarity 91.7%; Pred. No. 6.9e-56;
Matches 211; Conservative 9; Mismatches 10; Indels 0; Gaps 0;
QY 1 MSERKEGRGKGKKGKRGSGKPSAAGSQSPALPPOLKEMKSOESAAGSKLVLRCTSS 60
Db 1 MSERKEGRGKGKKGKRGSGKPSAAGSQSPALPPOLKEMKSOESAAGSKLVLRCTSS 60
QY 61 SEYSSLRPFKFWKGNELNRKNKPQNIKIQKPGKSELINKASLADSGEYMKVSKLGN 120
Db 61 SEYSSLRPFKFWKGNELNRKNKPQNIKIQKPGKSELINKASLADSGEYMKVSKLGN 120
QY 121 DSANITIVESNEITGMPASTEGAYVSSSPRISVSTEGANTSSSTSTTGTSHLV 180
Db 121 DSANITIVESNEITGMPASTEGAYVSSSPRISVSTEGANTSSSTSTTGTSHLV 180
QY 181 KCAEKEKTFVNGGECFMVKDLSNPSRYLCKPNEFTGDRCONVYMASFY 230
Db 181 KCAEKEKTFVNGGECFMVKDLSNPSRYLCKPNEFTGDRCONVYMASFY 230

RESULT 12

A56210
neu differentiation factor - rat (fragment)
C;Species: Rattus norvegicus (Norway rat)
C;Date: 02-Jul-1996 #sequence_revision 02-Jul-1996 #text_change 08-Sep-2002
C;Accession: A56210
R;Wen, D.; Suggs, S.V.; Karunakaran, D.; Liu, N.; Cupples, R.L.; Luo, Y.; Janesen, A.M.;
Mol. Cell. Biol. 14, 1909-1919, 1994
A;Title: Structural and functional aspects of the multiplicity of Neu differentiation fa
A;Reference number: A56210; MUID:94158863; PMID:7509448
A;Accession: A56210
A;Status: preliminary; translated from GB/EMBL/DBJ
A;Molecule type: mRNA
A;Residues: 1-230 <RES>
A;Cross-references: EMBL:U02315; NID:g408380; PIDN:AAA19940.1; PID:g408381
C;Superfamily: human heregulin; EGF homology; immunoglobulin homology

Query Match 31.6%; Score 1059; DB 2; Length 230;
Best Local Similarity 93.6%; Pred. No. 1.1e-53;
Matches 205; Conservative 4; Mismatches 10; Indels 0; Gaps 0;
QY 12 KGKKEGRGKGKKGKRGSGKPSAAGSQSPALPPOLKEMKSOESAAGSKLVLRCTSSSEYSSLRPFKWF 71
Db 1 KGKKEGRGKGKKGKRGSGKPSAAGSQSPALPPOLKEMKSOESAAGSKLVLRCTSSSEYSSLRPFKWF 60
QY 72 KNGNELNRKNKPQNIKIQKPGKSELINKASLADSGEYMKVSKLGNDSASANTTIVE 131
Db 72 KNGNELNRKNKPQNIKIQKPGKSELINKASLADSGEYMKVSKLGNDSASANTTIVE 131

Qy	515	-----NSLPASPIRUIVEDEYETTYEQYEPQAPVVKL-----ANGRAKRTK	556
Db	706	RGACALGSLGSLPASPFRIPIDEDDEYETTCQACPPPPRPRTRGASRTSAGPRWRRSR	765
Qy	557	PNGHIANR-----LEVDSNTSSQSSSESETDERVG---BDTPFLGIQNPL--AASL	604
Db	766	INGLAAQARAARADSLSSSGGSGSASASDDDDADDGALAEETPFLGURAHDAIURS	825
Qy	605	EATPAFRIADSRST	617
Db	826	DSFPPLCPAADSRT	838
RESULT 14			
JC5700			
C:Species: Homo sapiens (man)			
C>Date: 25-Nov-1997 #sequence_revision 25-Nov-1997 #text_change 09-Jul-2004			
C:Accession: JC5700			
C:Rigashiyama, S.; Horikawa, M.; Yamada, K.; Ichino, N.; Nakano, N.; Nakagawa, T.			
J. Biochem. 122, 675-680, 1997			
A:Title: A novel brain-derived member of the epidermal growth factor family th			
A:Reference number: JC5700; MUID:98006324; PMID:9348101			
A:Accession: JC5700			
A>Status: nucleic acid sequence not shown			
A:Molecule type: mRNA			
A:Residues: 1-850 <HG>			
A:Cross-references: UNIPROT:O14511; DBDJ:AB005060; NID:g2626738; PIDN:BAA23417			
A:Experimental source: SK-NSH cell			
C:Comment: This protein is a member of the epidermal growth factor family. It			
ating the differentiation of MDA-MB-453 cells.			
C:Superfamily: human erbB kinase activator alpha, brain and thymus; EGF homolo			
C:Keywords: glycoprotein			
F:258-311/Domain: Ig-like #status predicted <IG>			
F:345-381/Domain: EGF homology <EGF>			
F:346-381/Domain: EGF-like #status predicted <EGF2>			
F:147,278,451/Binding site: carbohydrate (Asn) (covalent) #status predicted			
Query Match 29.7%; Score 993; DB 2; Length 850;			
Best Local Similarity 37.1%; Pred. No. 3.3e-49;			
Matches 250; Conservative 98; Mismatches 189; Indels 136; Gaps 222			
Qy	11	GKGKKKRGSGKPKESAAGSQSPALPOLKEMKSOESAAGSKLVLCETSSSEYSSLLRPFKW	70
Db	218	GKNLKKVEGKILCTDCAT-----RPLKKMKSSQTQGVGEKOSLCKCEAAGNPQPSYRW	270
Qy	71	FKNGNELNRKNPNKIQTQKPGK--SELIRNKASLADSGEYCKVKISKLGNDSAGANIT	128
Db	271	FKDGKELNR---RDIRIKYGNRKNRSLQPNKVYKVEDAGEYCEAENILGKDTVRGL--	326
Qy	129	IVESNEIITGHPASTEGAYVSESPIRISVSTEGANTSSSTSTSTTGTSHLVKCAKEKT	188
Db	327	-----YV-----NSVSTLSSWSG--HARKCNETAKS	351
Qy	189	FCVNGGECFMVKDLSNPSRYLCKPNBFTGDRCONYVMAFYKHGLGFEFNAEELQKRV	248
Db	352	YCVNGGVCIYIEGINQLS---CKCPNGFTFGQRLEKULRLY--MPDPKQKABELQKRV	406
Qy	249	LTITGICALLVGMICVWAYCKTKKQKKLHDLRLQSLRSERNMMNIANGPHHPNPPP	308
Db	407	LTITGICVALLVGMICVWAYCKTKKQKQMHNLRLQNMCPAQH--RSLANGFSPHRLDP	465
Qy	309	ENVQLVQYVSKNVISSEHIVERAETSFPSTSHYSTTAHSHSTVTTQT-----PSHSWSNG	363
Db	466	ESIOMAD--YISKNPATDHWIRRETETTFGSGHSCSPSHRCSTATPTSSHRHESHTWSLE	524
Qy	364	HTESLTLSSESHVIMVSSVENSRSHESSPT--GGPRGLNGTGGPRECNFLRHARETP----	417
Db	525	RSELTSSQSGIIMLSSVGTSKCNPAACVBARARAAAYNLEE-----RRRATAPPYHDSV	580
Qy	418	DSYRDSPHSERVYAMTTPARMSPVDFTPTSPKPSPEMSPPVSSMTVSNPMSMA--VSPF	476

Db 581 DSLRDSPHSERVYVSLTTPARLSVDFHYSLATQVPTFEITSPNSAHAVSLPPAAPSIVR 640
 QY 477 MEERPLLLVTPRLREKXFDHP-----QQFSSFHNPADS-- 514
 Db 641 LAEQOPLL-----RHPAPPGPGPGPGPGADMQRSYYSYYPAAAGPGR 687
 QY 515 -----NSLPASPLRIVEDEEYETTOEYEPAPQPVKKL-----ANSRRAKRTK 556
 Db 688 RGTGALGSLGSLPASPFRIPEDDEYETTOEYETQECAPPPPRARGASRRTSAGPRWRRSR 747
 QY 557 PNHIANR-----LEVDSNTSSQSSNSESETEDETVG-----EDTPFLGIQNPPL-AASL 604
 Db 748 LNLAAQRAARADSLSLSGSGGGSASASDDDDADGALAAESTPFLGLRGAHALRS 807
 QY 605 EATPAFLADSR 617
 Db 808 DSPFLCFAADSR 820

RESULT 15
 JC5702
 ErbB kinase activator alpha2a, brain and thymus - rat
 C:Species: Rattus norvegicus (Norway rat)
 C:Date: 25-Nov-1997 #sequence_revision 25-Nov-1997 #text_change 09-Jul-2004
 C:Accession: JC5702; PC4417
 R: Higashiyama, S.; Horikawa, M.; Yamada, K.; Ichino, N.; Nakano, N.; Nakagawa, T.; Miyag
 J. Biochem. 122, 675-680, 1997
 A:Title: A novel brain-derived member of the epidermal growth factor family that interac
 A:Reference number: JC5700; MUID:98006324; PMID:9348101
 A:Accession: JC5702
 A:Status: nucleic acid sequence not shown
 A:Molecule type: mRNA
 A:Residues: 1-860 <HIG>
 A:Cross-references: UNIPROT:O35569; DDBJ:D89996; NID:G2605631; PIDN:BAA23345.1; PID:G260
 A:Experimental source: PC-12 cell
 A:Accession: PC4417
 A:Status: nucleic acid sequence not shown
 A:Molecule type: mRNA
 A:Residues: 'F', 212-213, 223-860 <H12>
 A:Cross-references: DDBJ:AB001576; NID:G2605478; PIDN:BAA23348.1; PID:G2605479
 A:Experimental source: PC-12 cell
 C:Comment: This protein is a member of the epidermal growth factor family. It is function
 ating the differentiation of MDA-MB-453 cells.
 C:Superfamily: human ErbB kinase activator alpha, brain and thymus; EGF homology; immun
 C:Keywords: glycoprotein
 F:274-327/Domain: Ig-like #status predicted <IGL>
 F:361-397/Domain: EGF homology <EGF>
 F:422-444/Domain: hydrophobic #status predicted <HYD>
 F:163,294,467/Binding site: carbohydrate (Asn) (covalent) #status predicted

Query Match 29.6%; Score 992; DB 2; Length 860;
 Best Local Similarity 37.2%; Pred.No. 3.8e-49;
 Matches 248; Conservative 99; Mismatches 190; Indels 130; Gaps 21;

QY 11 GKGKKKRGSGKKPESAGSQSPALPQPKEMKQESAAGSKLVLCETSEYSSLRPKW 70
 Db 234 GKNIRKEVGKILCTDCAT-----RPLKKMKSTQGEVGEKQSLKCEAAGNPPQPSYRW 286
 QY 71 FKNGLNLRKNPKQIKQKPKG--SELRINKASLADSGEYMKVSKLGNDSASANIT 128
 Db 287 FKDGKELNRS---RDRIKYNGRKNRSLQFNKVKVEDAGEYVCEAEINLGKDTVTRGLH 343
 QY 129 IVESNEIITGMPASTEGAYVSSPISVSTEGANSTSTSTSTGTSHLVKCAEKEKT 188
 Db 344 V-----NSVSTLSSWSG--HARKCNETAKS 367
 QY 189 FCVNGECMVKDLNPSRYLCKCPNEFTGDRCONVMASFYKHLGIFMEAEELYQKRV 248
 Db 368 YCVNGGVCVYIEGINQLS---CKCPNGFGQRCLEKPLRLY--MPDPKQAEELYQKRV 422
 QY 249 LTIITGICITALLVGVCMVAVCKTKKORKKLDRLRSLRERNMMNIANGPHHPNPP 308
 Db 423 LTIITGICITALLVGVCMVAVCKTKKORKKLDRLRSLRERNMMNIANGPHHPNPP 481

QY 309 ENVQLVQVSKNVLSSEHIVERAETSFTSHYTSTAHHSTTVTQT-----PSHSWNG 363
 Db 482 EBIQWAD-YISKNVFATDHVIRREAEITFGSHSCSPSHGCTATPTSSHRHSHTSLE 540
 QY 364 HTESILSESHSVIWMSSSVENSRHSPT--GGPRGLNGTGGPRECNFLRHARETP----- 417
 Db 541 RSELTSDSQGIMLSSVGTSCKNSPCVAREARRAAAYSOEE-----RRRAMPPYHDSI 596
 QY 418 DSYRDSPHSERVYVSLTTPARMSVDFHTSPSPKSPPESEMPPVSSMTVSMPSMA-VSPFF 476
 Db 597 DSLRDSPHSERVYVSLTTPARLSVDFHYSLATQVPTFEITSPNSAHAVSLPPAAPSIVR 656
 QY 477 MEERPLLLVTPRLREKXFDHP-----QQFSSFHNPADS----- 514
 Db 657 LAEQOPLL-----RHPAPPGPGPGADMQRSYYSYYPAAAGPGRGACAL 703
 QY 515 -----NSLPASPLRIVEDEEYETTOEYEPAPQPVKKL-----ANSRRAKRTKPNGHIA 562
 Db 704 GSGLSLPASFRIPEDDEYETTOEYETQECAPPPPRPRTRGASRRTSAGPRWRRSRLGLAA 763
 QY 563 NR-----LEVDSNTSSQSSNSESETEDETVG-----EDTPFLGIQNPPL-AASLEATPAF 610
 Db 764 QRARAARDLSLSSGSGGGSASASDDDDADGALAAESTPFLGLRAAHDALRSDSPPLC 823
 QY 611 RLADSR 617
 Db 824 PAADSR 830

Search completed: April 12, 2005, 14:42:49
 Job time : 50 secs